INVESTIGATING THE NEURAL NETWORKS INVOLVED IN EXTERNALIZING AND CONSCIENTIOUS BEHAVIOR

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Dedication

This dissertation is dedicated to friends and family who struggle with substance use and impulsivity despite their best intentions and kindest of hearts. May you be well, and may you be loved.

Abstract

Conscientiousness and impulsivity are traits that affect how well an individual is able to achieve their goals. Individuals high in Conscientiousness are described as being more industrious, maintaining order in their life, and having high self-discipline (Ozer & Benet-Martínez, 2006) and would likely score low on disinhibited externalizing. Individuals who score high on disinhibited externalizing behavior show lack of constraint, have higher sensation seeking behavior and are more prone to substance use (Miller, Lynam, & Jones, 2008). However, the neural systems underlying variation in these traits are not well understood. Functional connectivity is a way to study neural networks of the brain and can be used to assess whether or not individual differences are associated with connectivity in the brain.

Previous research shows positive associations between Conscientiousness and functional connectivity in the goal priority network (GPN; Rueter et al., 2018). Few studies have investigated associations between functional connectivity and Conscientiousness and disinhibited externalizing. In this dissertation, I: (1) attempted to replicate findings from a previous study with a larger sample to investigate associations between connectivity and Conscientiousness while extending the analysis to include disinhibited externalizing behavior and (2) apply the same functional connectivity methodology to a task-based fMRI data set to see if the traits of interest and connectivity remain associated during a cognitive task requiring inhibition. I hypothesized that the GPN and the central executive network (CEN) would be negatively associated with disinhibited externalizing behavior and that only the GPN would be positively associated with Conscientiousness.

Results from study one and study two suggest that the CEN is negatively associated with disinhibited externalizing, while only study two suggests that the GPN is negatively associated with disinhibited externalizing. Study two supported the hypothesis that the GPN is associated with Conscientiousness, while Study 1 did not. This dissertation provides an integrated investigation of how Conscientiousness and externalizing behavior are related on a biological level. Resisting impulses and orienting oneself towards goals are both important behaviors implicated in successfully navigating life. Further research on these networks may help us create therapies or treatments to increase Conscientiousness and reduce self-compromising, maladaptive, externalizing behaviors.

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<u>Chapter 1:</u> Introduction to Conscientiousness, Externalizing Behavior, and Neural Networks

> Soul and body, body and soul – how mysterious they were! There was animalism in the soul, and the body had its moments of spirituality. The senses could refine, and the intellect could degrade. Who could say where the fleshy impulse ceased, or the physical impulse began?
>
> -Oscar Wilde, *The Picture of Dorian Gray, 1891*

There are many reasons a person may be able to successfully achieve their goals. Some individuals may be able to maintain focus on immediate tasks to achieve long-term goals while others fall prey to impulsivity and disinhibition, favoring short term gains over long-term goals. In this dissertation, I examine personality traits relevant to goal attainment: Conscientiousness and disinhibited externalizing behavior. By investigating the neurobiological underpinnings of these traits, I hope to better understand why some individuals are routinely able at achieve their goals while others find it challenging to abstain from substance use or other disinhibited behavior.

Relevant Personality Traits

Personality traits are stable individual differences that reflect emotion, motivation, cognition and behavior. Therefore, personality traits may be used to predict how likely it is that someone will be able to achieve their goals or fall prey to impulsivity. Successfully achieving long term goals is associated with Conscientiousness, one of the “Big Five” personality dimensions, which describes the shared variance in traits like industriousness, orderliness, organizational ability, responsibility, and self-discipline (Ozer & Benet-

Martínez, 2006). A previous study using factor analysis found that Conscientiousness can be split into two distinct, but correlated, aspects, orderliness and industriousness (DeYoung, Quilty, & Peterson, 2007). These lower order traits represent a more fine-grained personality structure than the Big Five traits but are more broad than specific facets of personality (e.g. Conscientiousness facets in the popular NEO Personality Inventory–Revised include competence, order, dutifulness, achievement striving, self-discipline, and deliberation; Costa, & McCrae, 2008). Orderliness reflects the propensity for an individual to keep one's belongings neat and tidy and to keep one's life organized. Industriousness reflects the propensity to work hard and finish tasks, despite encountering challenges along the way. An individual who scores high in Conscientiousness will likely have high levels on the traits and behaviors listed above, while someone who scores high in disinhibited externalizing will likely score lower on the traits and behaviors listed above. Thus, one may think of Conscientiousness as the positive pole of the disinhibited externalizing spectrum while impulsive externalizing behavior highlights the more negative, maladaptive, pole.

Externalizing behavior can be described as a set of mental disorders and problem behaviors involving antisocial behavior, substance use, and personality traits such as aggression and impulsivity (Krueger, Markon, Patrick, & Iacono, 2005). Previous research suggests that externalizing behavior comprises a spectrum and that disinhibition and aggressive behaviors tend to occur together, making externalizing behavior a major dimension of comorbidity in psychopathology. Two traits are central to externalizing behavior: disagreeableness and unconscientiousness (Krueger, Markon, Patrick, Benning,

& Kramer, 2007; Miller et al., 2008). Disagreeableness is associated with aggression and antagonistic behaviors while unconscientiousness is associated with impulsivity. Behaviors that fall on the externalizing spectrum are typically negatively associated with being self-controlled, achieving long term goals, and behaving responsibly. In fact, behaviors such as committing crimes, taking illegal substances, acting aggressively, and engaging in risky sexual behavior all fall on the externalizing behavior spectrum (Miller et al., 2008).

Behaviors that fit under the Conscientiousness umbrella, such as achievement and self-control, are negatively correlated with specific externalizing behaviors such as problematic impulsivity as well as the externalizing spectrum broadly (Venables & Patrick, 2012). Many studies have suggested that Conscientiousness is positively associated with health and longevity, marital stability, academic and occupational achievement and monetary gains over the lifespan (Ozer & Benet-Martínez, 2006). Thus, it makes sense to think about a spectrum where Conscientiousness is on one pole and behaviors that are related to the disinhibited externalizing subfactor are on the other pole. The disinhibited subfactor contains traits like impulsivity, lack of constraint, sensation seeking and substance use. It is important to study both Conscientiousness and disinhibited externalizing behavior despite the fact that they are likely measures of the same latent dimension related to self control (Suzuki, Samuel, Pahlen, & Krueger, 2015). Previous findings from item response theory suggest that measures of Conscientiousness likely provide more information about variation at the middle and positive end of this spectrum while measures of maladaptive externalizing behavior likely provide more information about variation near the negative pole (Stepp et al., 2012). Given the importance of these traits on life outcomes, it is important to understand and investigate the neural underpinnings of the entire spectrum. One way to study neural underpinnings is to investigate the relations between traits and functional connectivity.

Studying functional networks in the brain

There are many ways to study how individual differences are associated with neural architecture and functional connectivity (the degree to which regions of the brain show synchronous neural activity; Mueller et al., 2013). Functional connectivity metrics allow researchers to use fMRI data from multiple subjects to establish a set of synchronously linked networks or nodes at the group level. After obtaining these group level networks, it is possible to extract connectivity metrics at the individual level, which can be used to study the relation between individual differences in neural networks and psychological traits.

Functional connectivity analyses can be more helpful in elucidating the relation between traits and the brain than other imaging techniques. Structural MRI studies are restricted to static morphometric values, and do not help us understand how the brain is functioning over time. Region of interest (ROI) based activation fMRI analyses constrain hypotheses to predicted regions of the brain and ignore fluctuations in neural activation in other parts of the brain. Many task-based fMRI studies use contrasts to compare neural activation during a specific task to neural activation during a similar control task, suggesting that the regions that are activated by both are unimportant. This may eliminate the study of many brain areas that are likely playing a role during both states. Functional connectivity studies do not require the researcher to include contrasts in their model and, depending on the statistical methods used, allow for spatially overlapping networks. Functional connectivity MRI (fcMRI) assesses fluctuations in blood oxygenation level (BOLD) signal and uses correlations among these fluctuations to identify brain regions that act in synchrony over time (Biswal, Yetkin, Haughton, & Hyde, 1995).

Currently, the most commonly used functional connectivity methods are based on independent component analysis (ICA). ICA methods report high levels of consistency in networks extracted across subjects as well as high consistency within subjects across multiple scans (Andrews-Hanna, Reidler, Sepulcre, Poulin, & Buckner, 2010; Damoiseaux et al., 2006; Meindl et al., 2010). When utilizing ICA methods, researchers extract intrinsic connectivity networks (ICNs) that act in synchrony in the brain but are maximally spatially independent of each other. This is done by implementing a standard preprocessing pipeline (like what one would use for any fMRI analyses) but then extracting group level networks determined by voxels' temporal correlations with one another, and applying these networks to subject-specific data (Friston, Frith, Liddle, & Frackowiak, 1993).

More specifically, ICA is a technique to decompose a two dimensional matrix (time x voxels) into a set of time-courses and their associated spatial components (Beckmann, DeLuca, Devlin, & Smith, 2005). Probabilistic ICA models include a parameter to model noise and are similar to a standard general linear model except that the mixing matrix is estimated from the data (as opposed to being a pre-specified prior). After creating these group-level, probabilistic, spatial components, dual regression is used to estimate individual-level connectivity metrics. This entails using group-level spatial maps as a set of spatial regressors to estimate individual *temporal* dynamics within each map. Then, these time courses are used as a set of temporal regressors to find subject-specific connectivity maps that are associated with group-level spatial maps. This process results in both *spatial network maps* and *corresponding timeseries* for each participant which can then be used to calculate total component inter- and intra-connectivity metrics.

Researchers are then able to compute a metric of *coherence* of individual networks (i.e., intra-connectivity, a measure of how correlated voxel activations are within a given network) and *interconnectivity* (i.e., a measure of how correlated one entire network is with another entire networks) for each ICN for each subject. Patterns of interconnectivity and coherence within networks are similar across task-based fMRI and resting state fMRI (Andrews-Hanna et al., 2010). These two measures of functional connectivity—coherence and interconnectivity—are based on "physiological coupling" within and between brain regions and reflect how BOLD signal changes moment-to-moment and how that signal varies over time (Menon & Uddin, 2010, p. 656). This coupling is considered "physiological" because it is linked to synchronous BOLD changes, but not "anatomical" which describes structural connections between regions via axons or white matter tracts. With coherence and interconnectivity data, it is possible to study general patterns of neural activity across a population as well as measures of individual differences in connectivity within these broad general patterns.

Much of the current functional connectivity literature focuses on resting state analyses, which analyzes brain activity over a period of time while a participant is lying awake in the scanner without engaging in a task. The arguments for studying resting state are often that ICAs conducted on resting state data are able to extract networks or components that can be linked to task performance (Biswal, Eldreth, Motes, & Rypma, 2010; Svensén, Kruggel, & Benali, 2002), even though the participant was not completing a task at the time of the scan. Thus, these studies tell us information about how the brain works in a generalizable way. For example, connectivity values derived from fMRI data collected during a working memory task were correlated with performance on the working memory task. Interestingly, connectivity values at rest in the same network were also correlated with performance on the same working memory task (Hampson, Driesen, Skudlarski, Gore, & Constable, 2006). Additionally, comparable functional architecture is found when assessing functional connectivity patterns of subjects who are asleep or under anesthesia (Vaidya & Gordon, 2013). Because of these stable patterns, researchers often find a common core of networks in the brain in each individual. These neural systems appear to help individuals process the world in both a modular way (e.g. the sensory cortex processes our sensory input) as well as in an interconnected way (e.g. the sensory cortex interacts with many other brain regions to relay that sensory input). Thus, ICA conducted on data derived from both resting state and task-based fMRI data can help researchers figure out how functional architecture supports individual differences in human behavior (Seeley et al., 2007).

In this dissertation, I use ICA exclusively because ICA is potentially more effective at detecting individual differences than clustering and seed-based approaches and it is able to isolate and remove artifactual connectivity patterns that may emerge in fMRI data (Smith et al., 2014). Extracting both group level networks as well as individual-level connectivity scores allows researchers to identify behavioral correlates of these core networks (Uddin, Supekar, & Menon, 2010). Meaningful associations between traits and patterns of connectivity exist in normal populations of individuals (Barch et al., 2013; Vaidya & Gordon, 2013), and previous work has shown that males and females have distinct connectivity patterns in resting state networks (Tomasi & Volkow, 2012). This highlights the importance of controlling for sex in studies on individual differences (Smith et al., 2014) and also provides evidence that brain function is associated with individual differences. Neural networks likely modulate real-world behavior and are related to why people differ in meaningful ways.

Core Networks in the brain

Previous studies of functional connectivity have found that the brain can be represented by common functional networks. These basic networks provide researchers a platform to study how connectivity varies between individuals (Smith et al., 2009) and how that variability may be related to personality traits. Researchers have identified associations between these networks and personality and other individual differences such as IQ (Adelstein et al., 2011; Heuvel, Stam, Kahn, & Pol, 2009; Kunisato et al., 2011).

A recent study used resting-state functional MRI scans of 1,000 healthy subjects to create parcellated maps of seven core networks (Yeo et al., 2011). The findings from this study suggest that the main networks in the brain include the following (labels were based on resemblance to previously described networks): visual, somatosensory, dorsal attention, ventral attention, central executive, limbic, and default. These seven core networks correspond to many of the networks discovered in previous studies. However, Yeo et al. (2011) also identified a stable 17-network solution, which appeared to fractionate the seven broad networks into smaller subnetworks. Most of these subnetworks stayed approximately within the same boundaries of the original seven network solutions, but a few showed reorganization of spatial boundaries.

The networks proposed by Yeo et al. (2011) were based on a clustering algorithm and were exclusive, meaning each voxel belonged to only one network. In ICA, components are not exclusive, meaning a single voxel can be in more than one component. Thus, the resulting components are unrestricted in size (though higher dimensionalities tend to yield smaller networks). While the networks reported by Yeo et al. (2011) have been invaluable in classifying and identifying networks, there are many benefits to allowing networks to overlap. First, allowing networks to overlap identifies patterns of covariation specific to the current sample. Second, allowing networks to overlap is a more realistic depiction of functional brain organization because one particular region may be involved in multiple networks (Marquand, Haak, & Beckmann, 2017). Lastly, allowing networks to overlap often fragments larger networks into empirically defined subnetworks which may be differentially related to traits or behaviors of interest.

In the present work, I focus on networks in the brain that are most likely to be associated with Conscientiousness and externalizing behavior: the central executive network (CEN) and the ventral attention and salience networks (VAN, SN). I also include brief reviews of the default network (DN) and dorsal attention network (DAN) because prior research has found associations between the DN and externalizing behavior (Castellanos, Kelly, & Milham, 2009) and because both the DN and DAN are located in similar regions as the CEN and VAN (Krienen, Yeo, & Buckner, 2014). See Figure 1.1 below for the illustration of Yeo et al.'s (2011) maps.

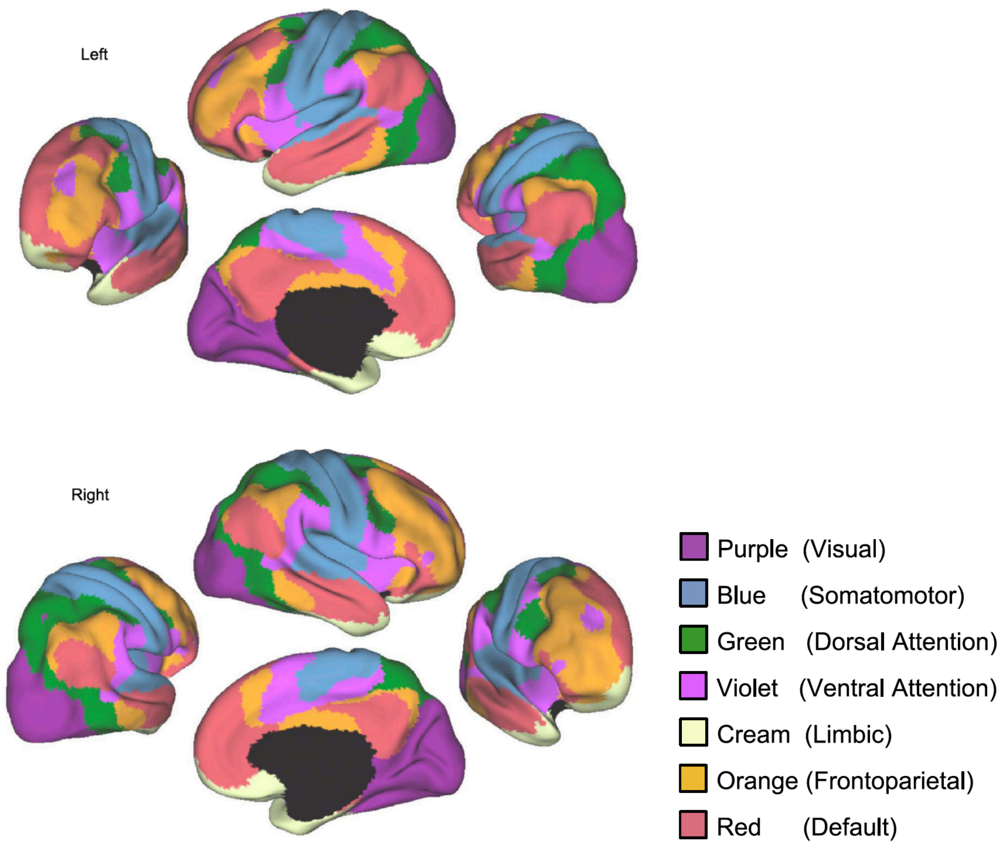


Figure 1.1. Yeo et al. (2011) functional network parcellation with key

Default Network.

The default network (DN), is a broad network that shows increased activity during passive states relative to most tasks and increased activity during tasks involving self-generated thought (Andrews-Hanna, Smallwood, & Spreng, 2014). For example, when individuals are completing a basic resting state scan (e.g., participants are asked to stay awake with their eyes open or closed) the DN is more active than when individuals are engaged in a difficult task involving attention to external stimuli. However, when individuals engage in behaviors like self-directed thought, perspective taking, episodic memory recall, thinking about the future, and using their imagination, the DN is also activated. This suggests that the DN is not only implicated in self-directed thought or active during the absence of most tasks, but that it plays a role more generally in engagement with self-referential memories or prospective cognition.

The DN comprises one core subsystem with two main hubs and two additional subsystems. The midline core subsystem has hubs in the posterior cingulate cortex plus adjacent precuneus and in the medial prefrontal cortex. The other two subsystems comprise: (1) the dorsal medial subsystem, involving dorsal PFC and regions of lateral temporal lobe, and (2) a medial temporal lobe subsystem. The midline core subsystem is often activated when individuals make emotional decisions that are relevant to both the present and future self. The medial temporal lobe subsystem shows activation when individuals make decisions that involve episodic simulation, as in replaying memories and creating images of their future self. The dorsal medial subsystem shows activation during activities that involve narrative comprehension and understanding the mental states of others. Individuals who appear to have an inability to deactivate their DN experience more lapses in attention, which likely leads to those individuals' committing more errors in tasks that require attention (Li, Yan, Bergquist, & Sinha, 2007; Weissman, Roberts, Visscher, & Woldorff, 2006). Additionally, inappropriate activation of the DN during tasks, where one would be more likely to see CEN activation, may be related to problems with sustained attention.

Central Executive Network.

The central executive network (CEN) is sometimes called the frontoparietal control network or the cognitive control network. This system has been described as the network that supports completion of cognitively demanding tasks that involve orienting attention to external stimuli. The CEN is spatially located within the dorsolateral prefrontal cortex (dlPFC), the anterior insular cortex, the posterior parietal cortex, the supplementary motor area, the inferior parietal lobe, and the dorsal anterior cingulate cortex (dACC; Cole & Schneider, 2007; Vincent, Kahn, Snyder, Raichle, & Buckner, 2008).

Previous research has found strong associations between the CEN and cognitive tasks such as working memory (D'Esposito et al., 1995; Menon & Uddin, 2010). Individuals "at rest" show increased activation in the DN relative to when people are engaged in cognitively challenging tasks, when they show increased neural activations in the CEN (Sridharan, Levitin, & Menon, 2008). Thus, the CEN and DN tend to be anti-correlated because most tasks elicit opposing responses in each the CEN and DN; for example, when a task requires more cognitive effort directed toward external stimuli, neural activity in the DN decreases while neural activity in the CEN increases. However, there are some tasks (e.g. The Tower of London) that show increased co-activation in both the DN and CEN, compared to baseline (Spreng, Stevens, Chamberlain, Gilmore, & Schacter, 2010). The tasks that show coactivation between the two networks require both complex cognitive processes as well as imagining future situations. Findings such as these suggest that the CEN plays a role in controlling attention in goal-directed behavior that aides in completion of challenging cognitive tasks (Menon & Uddin, 2010; Sridharan et al., 2008).

A recent meta-analysis of various executive functions found that flexibility, initiation, inhibition, and working memory all show similar activation patterns in the CEN (Niendam et al., 2012, total subjects = 2,832 across 193 studies). However, this study had a broad definition of the CEN. It included many different regions that had been identified during task-based fMRI studies, so the CEN was broader in this study than in some functional connectivity studies. Thus, it is important to look at the exact regions that they found for each executive function studied, given network maps like those of Yeo et al. (2011), which indicate that other networks in addition to CEN are also located adjacently in the lateral PFC, dACC, and parietal lobe. Flexibility, working memory, and inhibition were most closely associated with the dlPFC, cingulate, and superior and inferior parietal lobes. Initiation appeared to be related to both the CEN and regions frequently characterized as the SN. Thus, I explore the VAN and SN in the next section because both are implicated in completing cognitive tasks and goal-directed thought.

Ventral Attention Network and Salience Network.

Researchers have proposed that there is another, third, frontal network that acts as the “control switch” between the DN and CEN. The VAN is described as centering around the temporoparietal junction (TPJ) and right ventrolateral prefrontal networks, and specifically the right ventrolateral PFC (vlPFC; Fox et al, 2006; Vossel, Geng, &

Fink, 2014). The SN includes portions of the insula, orbitofrontal cortex and dorsal anterior cingulate cortex (dACC; Menon & Uddin, 2010; Seeley et al., 2007). The VAN reacts more strongly to task-relevant distractors than task irrelevant distractors, which may suggest that the VAN is implicated in successfully achieving long-term goals because it orients individuals toward potentially beneficial stimuli that they were not originally attending to (Fox, Corbetta, Snyder, Vincent, & Raichle, 2006). The VAN also plays a role in keeping one focused on the task at hand. Yeo et al. (2011) identified a broad VAN that is more extensive than what is typically described as VAN, including regions of dlPFC, insula, and dACC as well as TPJ and right ventrolateral prefrontal networks. Because this broader VAN includes areas that are associated with both the salience network and the traditional VAN, a new label is needed that suggests how these areas interact and combine to achieve a broader set of functions. For the remainder of this paper, I refer to this broad network encompassing both the VAN and the salience network as the goal priority network (GPN) (when referring to the VAN or salience network separately, I am referring to smaller networks as previously examined in the review.)

This GPN includes areas in both the VAN and SN and extends into the middle and superior frontal gyri, temporal operculum, the dlPFC, and the right vlPFC. I have chosen this label for this network because the VAN helps direct attention away from distractors and towards goals while the salience network integrates information about external stimuli to determine whether or not emotional, motivational, and interoceptive information is important to one's goals (Fox et al., 2006; Seeley et al., 2007; Uddin, 2015). Both of these networks work together to foster goal prioritization; one helps individuals ignore distractions and the other helps determine which stimuli in the environment is motivationally salient. It is likely that both of these networks interact and that the dlPFC component found in the broader GPN fosters the specific control necessary to achieve long term goals. I believe that the GPN plays a more complex role than simply “switching” one’s focus between external cognitive tasks (CEN) and self-referential thought (DN). The GPN is likely to be the network that prioritizes goals by determining whether or not the environment is necessitating outward, cognitive control abilities (CEN) or whether to look inward or think futuristically about one’s goals (DN). Thus, the efficiency of this network helps to determine how well individuals are able to achieve their long-term and short-term goals.

Supporting this conception, the GPN has been found to be related to Conscientiousness (Rueter, Abram, MacDonald, Rustichini, & DeYoung, 2018), but few studies have explicitly investigated associations between this network and Conscientiousness. A large meta-analysis investigated neural patterns that are associated with both global and domain specific executive function (Niendam et al., 2012). This study reported that the lateral and medial PFC (including the dlPFC) and the ACC are all related to executive function domains broadly (encompassing flexibility, inhibition, working memory, initiation, planning, and vigilance) which may suggest that regions of both the GPN and CEN are important in executing tasks and maintaining attention on the task at hand. However, this study also investigated domain specific neural patterns that may help distinguish regions associated with the GPN and CEN. Of the above domains, flexibility (described switching from one task to another or changing rules) was associated with the dlPFC, the dorsal cingulate cortex (DCC) and ACC, the superior and inferior parietal lobes, the insula, and inferior temporal gyrus. Inhibition (e.g. as measured by go/no-go tasks, Stroop tasks, and flanker tasks) was associated with the dlPFC, ACC, superior and inferior parietal lobes, frontal pole, and insula. Inhibition of motor responses is also associated with the vlPFC (Levy & Wagner, 2011). Based on the associations with the previous brain regions, flexibility may be closer to the role that the GPN plays while inhibition may be associated with the roles of both the GPN and the CEN.

Previous research has suggested that the dorsal attention network and GPN both reorient attention, but that the dorsal attention network is more involved with externally directed cognitive and sensory control (e.g. eye movements) towards specific stimuli, whereas the GPN is involved with reorienting attention in response to 'salient' sensory stimuli that may be beneficial to one's long term goals (Fox et al., 2006). In the next section I discuss the role of the dorsal attention network.

Dorsal Attention Network

The dorsal attention network (DAN) is associated with directing cognitive and sensory control towards an external source and is different from the GPN and CEN because it supports the tracking and processing of external, especially visual, stimuli. Some examples of this are shifting spatial attention, controlling eye movements, and managing hand-eye coordination (Corbetta & Shulman, 2002). It has also been shown to modulate the activity of visual areas of the brain (Vossel, Geng, & Fink, 2014). The CEN may play the role of "voluntary attentional controller" but the DAN supports the processes that are necessary when attention is directed outwards towards tasks. This network includes the following regions: ventral premotor cortex, superior parietal lobule, intraparietal sulcus, and the middle temporal area. While the GPN assesses saliency of stimuli in the environment and regulates attention in terms of one's long-term goals, the DAN assesses the perceived environment for cues that may be important for the currently operative goal by awaiting and detecting important visual and sensory targets. This network shows neural activity at the onset of search tasks (Astafiev et al., 2003). Over the course of a search task, activity in this network is maintained until the participant locates the target of the search, when the DAN shows a further increase in activity. Because this network is so closely implicated in directing sensory attention towards appropriate sensory cues, it is likely to be more present in task-based fMRI data relative to rest because it is typically more stimulus driven than resting state fMRI tasks.

Previous research on the neural underpinnings of Conscientiousness and Externalizing

Very few studies have reported associations between neural patterns and trait measures of Conscientiousness and disinhibited externalizing. Many of the published studies are underpowered, and due to current concerns surrounding replicability and reproducibility, I focus on correlational results between traits and fMRI studies with samples larger than 80 participants. I chose this threshold because a power analyses revealed that one would need 80 subjects to achieve power of .8 to detect effect sizes of r = .31 (assuming alpha = .05). This sample size threshold is too small to identify small effects, but until larger studies of neural correlates of traits are available, hypotheses must be based on the limited literature that is currently available. In all of the following sections, correlational findings associated with traits are generally reported only if sample sizes were sufficiently large. Studies designed to identify neural correlates of a specific task (e.g. a task-based fMRI study of the Go/No-Go task) are reported regardless of sample size because these research studies utilize contrasts between two states and have more power to detect effects than whole brain correlational studies.

Much of the fMRI research on externalizing behavior has focused on children and adolescents who have ADHD, which is a disorder comprising deficiencies in behavioral inhibition. While this reflects parts of the disinhibited externalizing spectrum, further research on trait disinhibited externalizing will be necessary in the future. While much of the fMRI research on these traits has been underpowered, structural studies of traits can be useful for identifying brain systems linked to traits. Many of these studies are sufficiently large and are relevant when making hypotheses about underlying neural mechanisms.

Structural MRI studies.

Previous research has shown positive correlations between the volume of regions in dlPFC and Conscientiousness (N = 116, DeYoung et al., 2010; N = 83, Jackson, Balota, & Head, 2011; N = 87, Kapogiannis, Sutin, Davatzikos, Costa, & Resnick, 2013; N = 507, Riccelli, Toschi, Nigro, Terracciano, & Passamonti, 2017 though see N = 265, Bjørnebekk et al., 2013; N = 227, Liu et al., 2013 for replication failures). Ricelli et al. (2017) found a significant, positive relationship between cortical thickness and Conscientiousness in the precuneus and the caudal middle frontal regions, which is in line with where we would expect to find nodes of the GPN or DAN. Damage to the dlPFC is associated with lower self-discipline (i.e. lower motivational stability) in traumatic brain injury patients compared to healthy controls (Forbes et al., 2014).

The most replicated findings in the ADHD literature suggest that children with ADHD have significantly smaller volumes in the dlPFC, caudate, pallidum, corpus callosum, and cerebellum than children without ADHD (Seidman, Valera, & Makris, 2005). Previous research on children has also found a negative linear association between the Child Behavior Checklist externalizing score and cortical thickness in the right cingulate, and the right medial temporal cortex, meaning that those with higher externalizing scores had lower cortical thickness values in these areas (N = 297, Ameis et al., 2014).

There are fewer studies on disinhibited externalizing behavior in adults. Previous research has found that impulsive-aggressive, male, personality disordered offenders had smaller temporal lobe volumes than control participants (N = 37, Dolan, Deakin, Roberts, & Anderson, 2002). A previous research study (N = 120; 60 cocaine users and 60 healthy volunteers) found that lower attentional control was associated with reduced volume in the insular cortex and increased volume of the caudate (controlling for years of cocaine use, frequency of cocaine use, and impulsive reward-seeking dimensions of impulsivity; Ersche et al., 2011). Additionally, more impulsive drug use was associated with reduced volume in the orbitofrontal cortex. These structural analyses allow researchers to investigate specific regions in comparison to traits, but do not directly measure brain function.

Task-based studies.

Task-based studies have explored the relations between both Conscientiousness and disinhibited externalizing and neural patterns. An EEG investigation reported that Conscientiousness is associated with increased right and left lPFC (broadly, because EEG is less spatially accurate than fMRI) activation during a go/no-go task (N = 106, Rodrigo et al., 2016). An fMRI study (N = 86) also found that Conscientiousness was associated with increased activation in the amygdala and insula while completing a "stressful" task in the scanner (Dahm et al., 2017). It should be noted that this task was similar to a typical intelligence test with an additional social pressure component to add pressure to the cognitive task. The dlPFC and insula, areas that have shown relations with Conscientiousness, are both found in the GPN and the CEN.

Many studies have shown associations between neural activity in the brain and states involving disinhibited behavior, but few have investigated trait disinhibition. The right inferior frontal gyrus (rIFG) shows increased activation at the same time as inhibitory control was elicited compared to baseline responding, suggesting that inhibitory control is related to rIFG activation (N = 81, Hampshire, Chamberlain, Monti, Duncan, & Owen, 2010). The right anterior insula (rAI) also plays a role in inhibition and in maintaining attention and focus during tasks at hand (N = 91, Ghahremani, Rastogi, & Lam, 2015). Additionally, during a go/no-go task as inhibition decreases, neural activity is reduced in the vlPFC and the dorsal amygdala (N = 58, Brown, Manuck, Flory, & Hariri, 2006). Given the previous findings, it appears that the CEN is most closely associated with impulsivity, updating and prepotent response inhibition. The GPN is likely related to Conscientiousness, impulsivity, shifting, and disinhibition.

Functional connectivity studies.

Functional connectivity studies have allowed researchers to investigate the relationship between traits and various networks in the brain; however, few studies have investigated the relation between Conscientiousness and neural connectivity. Rueter et al. (2018, N = 218) conducted the first direct test of how Conscientiousness is related to functional connectivity in the GPN. We found that coherence within a subnetwork of the GPN (a network comprising regions of the ACC, dlPFC, and insula) was positively correlated with Conscientiousness during a resting state scan. Resting state fMRI data are collected while a participant is lying in a scanner in the absence of any task or while completing a minimal task like pressing a button when a fixation cross occasionally changes color (to ensure wakefulness). Another study reported that Conscientiousness was positively associated with connectivity in a left CEN, in a right CEN, and in the DN during a resting state scan (N = 818, Toschi, Riccelli, Indovina, Terracciano, & Passamonti, 2018). Further analyses in this study reported that dutifulness and achievement (facets of Conscientiousness) were both positively associated with connectivity in the DN and dutifulness was positively associated with connectivity in the right CEN. The DN in this study included the frontal pole, medial prefrontal cortex, posterior cingulate gyrus, inferior parietal lobe, and the inferior frontal gyrus. The left frontoparietal network centered on the dlPFC with additional coverage of the inferior parietal lobe and medial superior frontal gyrus. The right frontoparietal network centered on the right frontal pole, inferior parietal lobe, with a small part in the middle temporal gyrus.

There are many more functional connectivity studies on disinhibited externalizing behavior than on Conscientiousness. Dysfunction related to ADHD has been proposed to be related to frontostriatal circuitry, and dysfunction in the vlPFC, dACC, and striatum (Bush, Valera, & Seidman, 2005). Much of the research on ADHD has been seed-based, and seed-based approaches introduce selection bias by investigators because the investigators select the seed location themselves using a priori hypotheses (Posner et al., 2014). Thus, much of the previous functional connectivity research on ADHD has used the dlPFC as the seed region. This is problematic because the dlPFC is involved in several different networks. When conducting functional connectivity studies utilizing independent components analysis (ICA), networks are temporally distinct, meaning they can share spatial characteristics over different time courses. Previous research has found that the dlPFC, although most often associated with CEN, is sometimes recruited by the DN, GPN, or DAN, depending on the task (N = 48, Krienen, Yeo, & Buckner, 2014); therefore, activation of the dlPFC does not necessarily indicate CEN activation. Because these networks are adjacent and partially overlapping, research centering on the dlPFC is not always able to distinguish which network is being reflected.

The insula has been described as the brain region that receives sensory, motor, and interoceptive information and combines it with emotional and cognitive information. This interaction supports awareness of the self, error-monitoring, and emotional and physiological states (Menon & Uddin, 2010). Impulsivity has been associated with connectivity in networks containing the insula (N = 218, Abram et al., 2015). In this study, general disinhibition and substance abuse were both positively associated with posterior insula coherence while general disinhibition was negatively associated with coherence in a network containing the anterior insula, ventral striatum, and cingulate. An additional study on cocaine addicts suggests similar connectivity patterns. Connectivity between a network containing the anterior insula and the ACC was lower in cocaine users compared to controls (N = 78, Wisner, Patzelt, Lim, & MacDonald, 2013). ADHD research has focused mostly on connectivity between the DN and CEN (Castellanos et al., 2009). However, the CEN and other networks in the PFC can overlap with the GPN, especially because spatial organization of these broad networks changes slightly depending on cognitive demands.

Based on the previous research, the GPN and the CEN are most likely related to disinhibited externalizing behavior and Conscientiousness. Importantly, the dlPFC appears to be related to both Conscientiousness and externalizing behavior. Krienen et al. (2014) found that these broad networks are located in generally the same position at rest as during tasks, but that the cortical locations and size of the networks differ slightly depending on the task that participants are completing in the scanner. When a seed was placed in the dlPFC across fourteen different tasks, researchers found that the dlPFC showed correlations with a network that included a large portion of the lPFC (broadly), the inferior parietal lobe, and the intraparietal sulcus across all tasks and was proposed as a typical CEN (Krienen et al., 2014). However, the shape of coverage of this network changed slightly depending on the task that was being completed in the scanner and the network was largest while completing a hard auditory task. When participants were completing a word-based 2-back task, the CEN was considerably smaller, suggesting that other networks may also be important when completing difficult cognitive tasks. Past research has also found ways to separate or pull apart regions of the CEN and GPN. One study trained a classifier to identify four distinct cognitive states (rest, retrieval of recent episodic memories, serial subtractions, silent singing of musical lyrics; Shirer et al., 2012). While this research is not specific to the CEN and GPN, there were regions of the dlPFC and insula that exhibited within network and between network connectivity changes depending on the task that was administered. This suggests that different networks are recruited when individuals complete different tasks, and may suggest that different traits are related to different networks. To fully understand how the GPN and CEN are functioning, we must study connectivity from many states (e.g. from both resting state and across different tasks) to be able to distinguish whether or not we are observing stable network properties or contributions from networks that vary depending on the task being completed.

Present studies

There are limitations to the existing research on the neural correlates of traits like Conscientiousness and disinhibited externalizing behavior. Importantly, few studies have looked at the relation between trait Conscientiousness and functional connectivity. Of the studies that have assessed the relationship between disinhibited externalizing behavior and functional connectivity, many of them were conducted on children or on individuals with diagnoses (e.g. addiction or ADHD). Lastly, no studies have analyzed how

Conscientiousness and disinhibited externalizing behavior are related to functional connectivity using the same methods in the same sample.

In this dissertation I use ICA to: (1) replicate previous findings by Rueter et al. (2018) that GPN connectivity is related to Conscientiousness during rest; (2) extend previous findings by investigating whether or not GPN connectivity is inversely related to externalizing behavior during rest; (3) visualize the functional architecture and spatial distribution of the CEN and GPN while individuals complete a cognitive control task in the scanner, and (4) investigate associations of Conscientiousness and disinhibited externalizing with connectivity during a task-based fMRI scan that elicits cognitive control.

Chapter 2: Resting State Functional Networks and the Conscientiousness-Disinhibited Externalizing Spectrum

Introduction

Two of the Big Five traits play a role in externalizing behavior: disagreeableness and unconscientiousness (Krueger et al., 2007). Disagreeableness is associated with aggressive behaviors while unconscientiousness is associated with impulsivity. The aim of the current investigation is to study individual differences in goal achievement and self-control; thus, I focus on disinhibited externalizing as it is related to Conscientiousness. Even though many studies have been conducted on externalizing behavior broadly, few studies have investigated both Conscientiousness and disinhibited externalizing together in functional connectivity studies. Disinhibited externalizing can be conceptualized as low Conscientiousness but has an explicit emphasis on dysfunction. By investigating both disinhibited externalizing behavior and Conscientiousness in the same sample I hope to better understand the neural systems that underlie both traits, and to better understand how goal-prioritization and impulsivity are related to various functional networks in the brain.

Functional connectivity MRI (fcMRI) assesses correlations of fluctuations in blood oxygenation level (BOLD) signal to identify brain regions that act in synchrony over time (B. Biswal et al., 1995). Resting state functional connectivity metrics allow researchers to investigate relations between individual differences in functional connectivity and individual differences in traits. It has been proposed that functional connectivity analyses are more helpful in understanding how the brain may function in real life, relative to structural and activation-based fMRI analyses, because structural analyses are restricted to static morphometric values and activation-based analyses typically constrain hypotheses to predicted regions and ignore fluctuations in neural activation in other parts of the brain or in the brain as a whole. Typical fMRI studies, targeting activation, require contrasts to compare neural activation during a task to neural activation during rest/fixation or a control task; however, functional connectivity studies do not require the researcher to include contrasts in their model.

As discussed in the previous chapter, two broad networks that are most conceptually relevant to Conscientiousness and disinhibited externalizing are the CEN, because it supports completion of cognitively demanding tasks, and the GPN because it supports prioritization of goals by determining whether or not stimuli in the environment should be given attention based on motivations, goals, and the current cognitive task. Individuals who score higher in Conscientiousness may have higher levels of connectivity within the GPN and individuals higher in externalizing behavior may have lower levels of connectivity in the GPN. Additionally, individuals who exhibit more disinhibited externalizing behavior may have lower levels of connectivity within the CEN. For reasons that will become clear after reviewing relevant literature, I did not hypothesize that connectivity within the CEN would be related to Conscientiousness, despite the previous hypothesis that they would be related to disinhibited externalizing.

Because few studies have investigated the neural correlates of Conscientiousness and disinhibited externalizing traits, a brief overview of behavioral correlates of Conscientiousness and externalizing behavior may help to interpret the available neurobiological literature. Individuals with higher Conscientiousness complete the Wisconsin Card Sort Task (WCST) more efficiently than individuals with lower Conscientiousness (Jensen-Campbell et al., 2002, N=113). In fact, individuals with higher Conscientiousness not only learned more efficiently, they were more also more likely to maintain a successful sorting strategy that they developed early while completing the task. This suggests that Conscientiousness is related to many facets of goal achievement, including perseverance, inhibition, and efficiency. On the other side of the spectrum, individuals who are characterized as impulsive generally choose smaller sooner rewards over larger later rewards (Hamilton et al., 2015). Studies show that abusers of many drugs, including alcoholics, are more likely to choose smaller, sooner rewards (Kirby Kris N. & Petry Nancy M., 2004; Lejuez C.W. et al., 2010; Petry, 2001). In a study of school aged children (ages 6 and 8, N= 169), level of impulsive behavior on a laboratory-based cognitive task predicted both maternal- and self-ratings of externalizing behavior across adolescence (Olson, Schilling, & Bates, 1999). These behavioral studies highlight the similarities between Conscientiousness, externalizing behavior, and their potential relation to different aspects of executive function.

Executive function (EF) is a broad construct that reflects various mental control processes that help with self-regulation (Leary & Tangney, 2012). Some researchers have broken down executive function into three primary EFs including updating, shifting, and inhibition (Miyake & Friedman, 2012) and others have broken down EF into more specific domains including initiation, inhibition, working memory, flexibility, planning, and vigilance (Niendam et al., 2012). These functions are a group of conscious cognitive control processes that help regulate human thought and behavior. The relation between updating and goal maintenance or inhibition and goal maintenance may be more intuitive than the relationship between shifting and goal maintenance; simply put, a person must inhibit distracting impulses and update their working memory to adequately complete the difficult cognitive tasks that help orient them towards their goals. However, in order for an individual to be successful at maintaining long-term goals an individual must sometimes favor more salient or relevant goals over other short-term, irrelevant goals. In this way, shifting between different mental states and abandoning less important task goals is a crucial cognitive process in achieving long-term goals. Individual differences in EF have been associated with successfully implementing a dieting regimen and meeting exercise goals (Hall, Fong, Epp, & Elias, 2008).

The working memory component of EF most closely reflects the ability to maintain and manipulate information in short term memory. Working memory is necessary for active problem solving as well as monitoring one's surroundings. A very large study (N = 47,519) reported that individuals who scored low on Conscientiousness experienced more executive function problems, but that Conscientiousness was not associated with working memory performance (Buchanan, 2016). This suggests that neural correlates of EF may be informative to the current hypotheses. The CEN covers much of the lPFC, especially the middle frontal gyrus, and is associated with IQ and working memory (Baddeley, 1996; Collette & Van der Linden, 2002; Tanji & Hoshi, 2008). Conscientiousness (and closely related traits, like Grit, that can be described as facets of Conscientiousness) is generally unrelated to working memory and intelligence

(DeYoung, 2011; Duckworth, Peterson, Matthews, & Kelly, 2007). Thus, a different domain of EF likely contributes to Conscientiousness. However, previous research reports either a negative correlation between Conscientiousness and EF tasks (Unsworth et al., 2009) or no relation at all (Murdock, Oddi, & Bridgett, 2013; Williams, Suchy, & Kraybill, 2010).

Research by Fleming, Heintzelman, & Bartholow (2016) attempted to tackle the question of how Conscientiousness fits into the EF framework directly. They administered nine EF tasks that were able to distinguish between working memory updating, mental set shifting, and response inhibition (N = 420). Using structural equation modeling, they were able to show that Conscientiousness is most closely associated with shifting—that is, flexibility and the ability to adapt to changing task demands. This shifting component may reflect more of the salience, or goal priority components, of EF.

A meta-analysis of EF found that flexibility, initiation, inhibition, and working memory all show similar activation patterns in the frontal and parietal regions including the dlPFC, ACC, inferior and superior parietal lobe, and precuneus (Niendam et al., 2012 total subjects = 2,832 across 193 studies). Shifting, or flexibility, appeared to be most closely associated with the dlPFC, superior and inferior parietal lobe, and in areas of the occipital and temporal lobe. Inhibition and initiation showed associations with activation in the dlPFC, ACC, motor cortex, superior and inferior parietal lobes, as well as some regions of the caudate, thalamus, and putamen. The right inferior frontal gyrus (rIFG) also shows associations with inhibitory control (N = 81, Hampshire, Chamberlain, Monti, Duncan, & Owen, 2010). Working memory tasks elicited activation in the dlPFC and parietal lobe. Of note, the dlPFC played a role in all types of EF, which complicates the potential relationship between the neural underpinnings of Conscientiousness and impulsive externalizing behavior.

Research on response inhibition may help solve this puzzle. Response inhibition is consistently associated with frontal cortex activation, but both the GPN and CEN are represented in the frontal cortex (Ridderinkhof, van den Wildenberg, Segalowitz, & Carter, 2004; Simmonds, Pekar, & Mostofsky, 2008). Researchers discuss inhibition as having two components, (1) motor response inhibition or prepotent response inhibition, and (2) goal-directed, intentional inhibition that occurs via response selection. These two types may be associated with the CEN and GPN, respectively. The distinction between the two types of inhibition is important because *intentional* inhibition first involves inhibiting other prepotent responses and then selecting a new response (Simmonds et al., 2008). The difference between prepotent response inhibition and intentional inhibition is temporal, in that prepotent response inhibition occurs first and intentional inhibition (which allows an individual to select a different goal or response) happens later. During tasks that require prepotent response inhibition (e.g. Go/No-go tasks), activation is seen in the inferior parietal lobes, insula, dlPFC, middle frontal gyrus, rIFG, and medial prefrontal cortex (Liddle, Kiehl, & Smith, 2001; Simmonds et al., 2008). These regions are found in both the CEN and GPN. A functional connectivity study suggests that prepotent response inhibition is related to connectivity between the CEN and the salience network (Leech, Kamourieh, Beckmann, & Sharp, 2011). The dlPFC, vlPFC, and dorsal medial frontal cortex have also shown relations with short-term memory representations of goal-directed behavior, intentional inhibition, and internally guided inhibition, which is in line with how the GPN has been characterized in previous research (Aron, Robbins, & Poldrack, 2014; Kühn, Haggard, & Brass, 2008; Lynn, Muhle-Karbe, & Brass, 2014; Ridderinkhof et al., 2004; Rueter, Abram, MacDonald, Rustichini, & DeYoung, 2018; Schel, Scheres, & Crone, 2014). A large-scale, neural-based meta-analysis suggests that both the GPN and CEN are recruited by inhibition tasks (Zhang, Geng, & Lee, 2017). Interference resolution, which entails attending to information based on relevance to an ongoing task and also suppressing irrelevant distractions, is most closely associated with the GPN. Prepotent response inhibition (specifically action cancellation or action withholding) implicated both the GPN and the CEN. These findings suggest that the GPN may be associated with both types of inhibition while the CEN may only be associated with prepotent response inhibition.

I predict that low GPN functional connectivity is associated with low Conscientiousness and is associated with disinhibited externalizing. I also predict that low CEN connectivity is associated with the disinhibited externalizing spectrum. When an individual has low connectivity in the GPN and CEN, these levels of disinhibited externalizing may approach dysfunctional levels. I propose that the GPN is related most closely to the shifting domain, but that inhibition may also be related to GPN function. Previous research supports these hypotheses. Rueter et al. (2018) found that functional coherence within a network encompassing regions of dlPFC, ACC, and insula was positively correlated with Conscientiousness. These areas of the brain were associated with inhibition in previous EF studies as well (Niendam et al., 2012). Dysfunction related to ADHD has been proposed to be related to dysfunction in the dlPFC, dACC, and striatum (Bush et al., 2005) and has been characterized as stemming from prepotent response inhibition (Slaats-Willemse, Swaab-Barneveld, de Sonneville, van der Meulen, & Buitelaar, 2003). These findings suggest that disinhibited externalizing may be related to both the GPN and CEN.

In this study, I attempt to replicate and extend the findings of Rueter et al. (2018) using a large, publicly available data set from the Human Connectome Project. Additionally, I will extend the investigation by assessing whether or not there are associations between disinhibited externalizing behavior and connectivity in the GPN and the CEN. I hypothesize that individuals who score higher in Conscientiousness will have higher levels of coherence and interconnectivity within the GPN and individuals higher in externalizing behavior would have lower levels of coherence and interconnectivity in the GPN. I also hypothesize that connectivity and coherence in the CEN during rest will not be related to Conscientiousness but may be weakly negatively related to externalizing. Coherence and interconnectivity in the CEN may be related to impulsive externalizing behavior because IQ and externalizing are typically weakly negatively correlated (Andersson & Sommerfelt, 2001; Lynam, Moffitt, & Stouthamer-Loeber, 1993) and also because the CEN covers much of the lPFC which is most closely associated with IQ and working memory (Baddeley, 1996; Collette & Van der Linden, 2002; Tanji & Hoshi, 2008). In contrast, Conscientiousness is generally unrelated to intelligence (DeYoung et al., 2011). This study also has the potential to clarify how the CEN and VAN interact to support positive behaviors that lead to vocational and educational success.

Methods

Participants: Participants for the first study were recruited by the Washington University – University of Minnesota Human Connectome Project (WU-Minn HCP; N = 1200; Van Essen et al., 2013). These subjects were drawn from a healthy population of monozygotic and dizygotic twins as well as their non-twin siblings (age range: 22-35 years). This age range was recruited because these individuals have likely already gone through major neurodevelopmental changes associated with adolescence and young adulthood but have not yet experienced the onset of neurodegenerative changes associated with aging (Van Essen et al., 2012). Exclusions for participation included the following: individuals with siblings who have severe neurodevelopmental disorders, individuals diagnosed with neuropsychiatric conditions, or individuals with neurological disorders. The sample includes individuals who choose to smoke, are overweight, and have a history of heavy drinking or recreational substance use, which is beneficial for the current study of impulsive externalizing behavior. Substance use and heavy drinking are associated with disinhibited externalizing behavior and the sample is likely to include most of the range of the Conscientiousness-Disinhibited Externalizing spectrum. Of the 1200 participants who were enrolled in the study, only participants who completed 4 full resting state fMRI runs were included in the resting state functional connectivity analysis. The final participant count for the resting state analysis is N = 1003, and the final participant count for the current study is N = 985 due to missing data on the following variables: 2 participants missing personality questionnaires, 12 participants missing intelligence measures, and 3 participants missing externalizing measures. Subjects without personality, externalizing, or intelligence measures were excluded from the study.

Personality Questionnaires: The NEO-FFI (a 60 item, shorter version of the NEO-PI-R) was used to measure the Big Five. While Conscientiousness is the main Big Five trait of interest, I controlled for the other Big Five traits while conducting analyses to make sure that network associations with Conscientiousness were specific to the trait.

Externalizing Measures: The Achenbach Adult Self-Report (ASR) was administered to participants. This questionnaire is self-administered and is a revision of the Young Adult Self-Report questionnaire (YASR; Achenbach, 1997). Previous researchers have factor analyzed the ASR and were able to create distinct Externalizing subscales (including attention problems, aggressive behavior, and rule-breaking behavior and intrusiveness) and DSM-IV categorical subscales related to attention deficit/hyperactivity (including an inattention subscale and hyperactivity-impulsivity subscale; Achenbach, Bernstein, & Dumenci, 2005; Miller, Lynam, & Jones, 2008). The main measures of disinhibited externalizing used in the current study include: ASR rule-breaking behavior, DSM-IV inattention, DSM-IV hyperactivity-impulsivity subscale, and DSM-IV ADHD (which combines the DSM-IV inattention and hyperactivity subscales).

Previous studies have reported that inattention-disorganization type traits were most closely associated with Conscientiousness out of all of the Big Five (Nigg et al., 2002), which would mean that they would fall on the Conscientious-Disinhibited

Externalizing spectrum. Previous research has reported that rule-breaking behavior is associated with Conscientiousness (Mount, Ilies, & Johnson, 2006). The ASR includes a general externalizing scale, but this includes both aggression and impulsivity measures, which means it reflects a blend of disagreeableness and unconscientiousness. Thus, this measure is not well-suited to testing hypotheses specifically about disinhibited externalizing. I used the DSM-IV ADHD scale as the main index of disinhibited externalizing because it is negatively correlated with Conscientiousness, which reflects the expected relation. I did not include ASR Rule-Following in the overall index of disinhibited externalizing because it was more strongly correlated with Agreeableness than Conscientiousness.

Intelligence: Participants in this study sample have completed many cognitive tests that measure intelligence. The HCP used the NIH Toolbox of Cognition measures, which includes measures of intelligence that are commensurate with the WAIS-V. The NIH Toolbox of Cognition includes measures of both verbal intelligence subtests (picture vocabulary and reading recognition) and nonverbal, “fluid” intelligence subtests (dimensional change card sort, flanker task, picture sequence memory, list sorting, and pattern comparison.) The age-adjusted cognitive function composite scores were used in this study. This measure of intelligence will be included as a covariate because intelligence is often weakly negatively correlated with Conscientiousness and is correlated with resting state connectivity (Cole, Yarkoni, Repovš, Anticevic, & Braver, 2012; Song et al., 2008; Wang, Song, Jiang, Zhang, & Yu, 2011).

Motion parameters: Motion during MRI was included as a control variable because it can cause spurious correlations between components in ICA (Power, Barnes, Snyder, Schlaggar, & Petersen, 2012). I used root-mean-squared (RMS) movement as an index of motion. This is a summary statistic that takes into account the average movement or change across six different parameters (including translational displacement across X, Y, and Z axes and rotational displacements across pitch, yaw, and roll; Marcus et al., 2013).

Image Acquisition: Researchers acquired resting-state functional MRI scans using a 3T Siemens Connectome Skyra scanner at Washington University. Participants completed four runs (each approximately 15 minutes). During the scan, participants were instructed to keep their eyes open and to maintain a relaxed fixation on a bright cross-hair on a dark background.

Scan sequence parameters were as follows: multiband accelerated gradient-echo echo-planar imaging of 1200 volumes; repetition time (TR) = 720 ms; echo time (TE) = 33.1 ms; flip angle = 52°; voxel size = 2 x 2 x 2 mm (Smith, et al., 2013). Multiband was used because it allows for faster data collection, more dense temporal sampling of physiological confounds and because it offered "richer temporal characterization of resting-state fluctuations" (p. 146).

Preprocessing and ICA Procedure: The HCP pipeline has already completed ICAs for individuals who had four complete fMRI runs. Pre-processing steps included: head motion and distortion (B0) correction, registration (aligning the timeseries to the structural data), and resampling the EPI sequences into standard space (2mm MNI space;

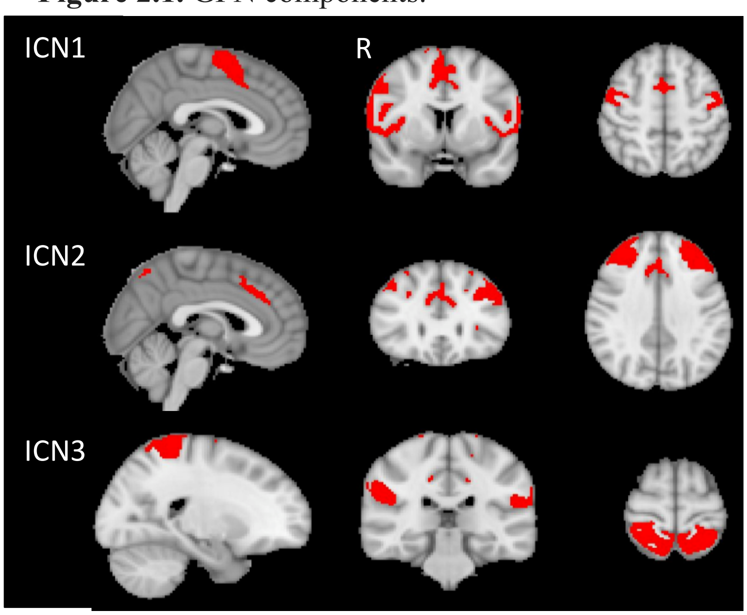
Smith et al., 2013). Global intensity normalization was also applied, and the non-brain voxels were masked out. Temporal pre-processing was conducted by applying highpass filtering (using -bptf option of FSL's fslmaths tool) with a cutoff of 2000s (FWHM= 2355s; note that the data length is 864 s/run). No lowpass filtering was applied. ICA was run on all subjects by using MELODIC and then fed into ICA-FIX to classify components as "good" or "bad" at the subject level. "Bad," often called "artifactual," components were regressed out of the timeseries at the subject level, and thus, the resulting components should include fewer artefacts and contain less noise (Smith, S. et al., 2013). All of these steps were run using volumetric data rather than surface space because many artifacts are 3D and do not respect tissue boundaries which may be related to functional properties of brain regions. MELODIC and ICA-FIX were conducted in various dimensionalities (i.e. dimensionalities reflect the number of components extracted from ICA); in this analysis, I use the dataset that extracted 50 components because previous research suggests this dimensionality provides the most reliable, robust, and replicable values (Poppe et al., 2013).

Component Selection: Classifying networks is the first step of conducting my analysis, given my specific, network-based hypotheses. I used percentage of cortical overlap of each ICN with the parcellations for GPN, CEN, DN, and DAN identified by Yeo et al. (2011) to identify which components corresponded most closely to each network. The components with the highest overlap with each network were then visually inspected to verify that they correspond well to each network—that is, their clusters were centered on the networks identified by Yeo et al. (2011). The set of 50 components has three components that distinctly reflect the GPN (ICNs 1 – 3), five components that reflect the CEN (ICNs 4 – 8), eight components that reflect the DN (ICNs 9 – 16), and three components that distinctly reflect the DAN (ICNs 17-19).

The networks that are central to our hypotheses include the GPN and CEN. Within the GPN, ICN 1 includes regions of the anterior cingulate cortex, temporal operculum, and insula. ICN 2 includes the middle frontal gyrus (including the dorsal lateral prefrontal cortex), frontal pole, and the paracingulate gyrus. ICN 3 includes regions of the precuneus, temporal operculum and the superior parietal lobe. See Figure 2.1 (below) for visualizations of the GPN components.

Within the CEN, ICN 4 is a right lateralized network comprising the paracingulate gyrus, posterior parietal cortex, frontal pole, supplementary motor area and middle temporal gyrus. ICN 5 is a left lateralized network comprising the middle frontal gyrus,

Figure 2.1. GPN components.



supramarginal gyrus, and the frontal pole. When visually and quantitatively assessing ICN 5, it appears to be a combination of the CEN and GPN, which is important while interpreting any results including this network. ICN 6 is a bilateral network that includes the posterior parietal cortex, middle temporal gyrus, and the middle frontal gyrus. ICN 7 includes the posterior cingulate cortex and the precuneus, and ICN 8 is a bilateral network comprising the superior frontal gyrus, middle frontal gyri, and bilateral frontal poles. See Figure 2.2 (next page) to for visualizations of the CEN components.

One network (ICN 9) appears to be a combination of the DN and GPN, and thus, I will be using this network in my analysis. ICN 9 is a right lateralized network comprising the superior frontal gyrus, middle frontal gyrus (and also dlPFC), and medial temporal lobe. It includes the DN as well as areas within the GPN (see visualization of ICN9 in figure 2.3 next page). The remaining networks in the DN and DAN are not explained in detail because the DN and DAN networks will be used only in the partial correlation analyses as control variables.

Functional Connectivity Metrics: Connectivity metrics within each component (coherence) were computed and provided by HCP. This functional connectivity metric reflects the average correlation of each vertex (described as a 2D voxel) in a given component with the mean time-series for all vertices in that component for each subject (this is computed using subject-specific spatial maps derived via dual regression). Interconnectivity between each component (interconnectivity) was computed as the correlation (Fisher z-transformed) between the mean time series of each pair of components for each subject (again using subject specific timeseries derived via dual-regression).

Figure 2.2. CEN components.

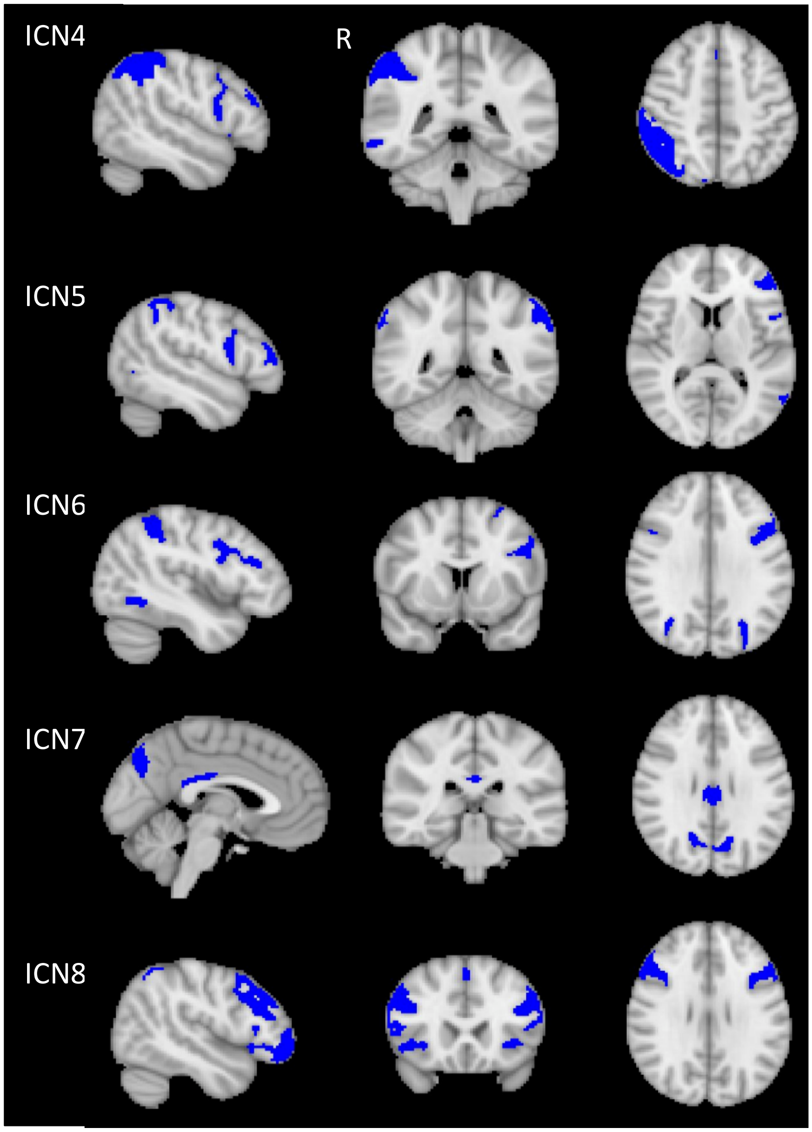
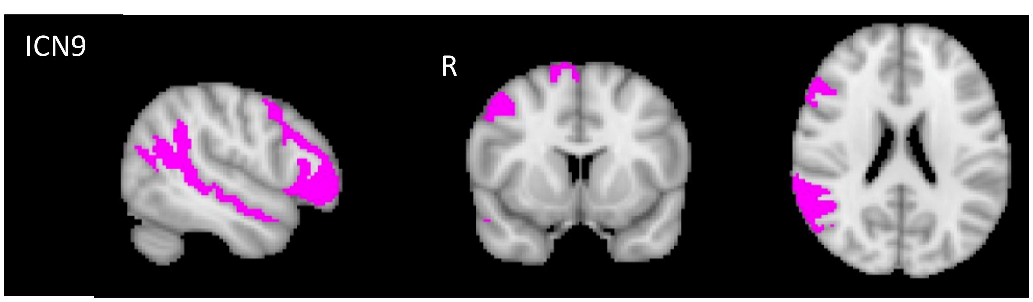


Figure 2.3. Component 9.



A power analysis revealed that, assuming alpha = .05, this sample (N = 985) will have a power of .9 to detect effect sizes of r = .1 or stronger. This suggests that I was able to detect smaller effects with similar or greater power than Rueter et al. (2018).

Results

See Table 2.1 (next page) for descriptives and zero-order correlations for the behavioral variables in the current study.

Connectivity and Conscientiousness:

Coherence and Conscientiousness. I hypothesized that coherence in the GPN during rest would be positively associated with Conscientiousness and that coherence in the CEN during rest would not be associated with Conscientiousness. To test these hypotheses, I ran partial correlations controlling for age, sex, IQ, motion, and the other ICNs that occupied similar regions. That is, I controlled for ICN coherence in the CEN, DN, and DAN when assessing the relation between the GPN and Conscientiousness and I controlled for ICN coherence in the GPN, DN, and DAN when assessing the relation between CEN and Conscientiousness.

There were no significant associations between GPN ICN coherence and Conscientiousness (see Table 2.2 for associations with C and the rest of the Big Five), which was also true when controlling for the other Big Five traits. ICN5 (a network that was classified as the CEN according to visual and quantitative inspection) coherence was correlated with Conscientiousness (partial r = - .087, p = .007), which does not support my hypothesis. This effect remained significant after controlling for all other Big Five traits and after Bonferroni correction for multiple tests. I chose to correct only for the

Table 2.1. *Descriptives and zero-order correlations among behavioral variables.*

Variables	C	A	N	O	E	IQ	ASR rf	DSM adhd	DSM inatt	DSM hyp
Conscientiousness	-									
Agreeableness	.22	-								
Neuroticism	-.41	-.29	-							
Openness	-.51	.08	.02	-						
Extraversion	.27	.29	-.35	.09	-					
IQ	-.12	.08	-.13	.26	-.02	-				
ASR Rule Following	-.34	-.37	.25	.17	-.05	-.08	-			
ASR Externalizing	-.32	-.48	.39	.12	-.02	-.05	.82			
DSM ADHD	-.53	-.30	.42	.08	-.08	-.02	.54	-		
DSM Inattention	-.60	-.22	.42	.08	-.14	-.02	.43	.90	-	
DSM Hyperactivity	-.30	-.31	.32	.06	.01	-.02	.53	.86	.55	-
Mean	34.39	33.51	16.53	28.48	30.68	114.3	2.55	5.69	3.19	2.50
SD	5.91	5.82	7.36	6.19	6.00	20.13	2.82	3.89	2.38	2.03

Notes. N = 985. All correlations greater than .06 in absolute value are significant at $p < .05$

multiple tests of association with Conscientiousness because our hypotheses are specific, and these are the tests where I risk supporting my hypothesis through Type I error. I ran partial correlations between the other Big Five traits and the networks of interest to investigate whether or not Conscientiousness is specifically associated with CEN and GPN networks. It is worth noting that Openness/Intellect (a trait reflecting cognitive exploration and intelligence) was associated with the CEN ICN7 (partial $r = -.086$, $p = .008$). This association remained significant after controlling for the all other Big Five traits, including Conscientiousness.

Table 2.2. *Partial correlations between the Big Five and coherence of components in GPN and CEN, controlling for the other Big Five traits, age, sex, IQ, motion, and components in DN, DAN, and either CEN or GPN.*

	C	A	N	O	E
GPN Component					
ICN 1	.02	.00	-.03	-.02	-.02
ICN 2	.02	-.02	-.05	.02	-.02
ICN 3	.01	-.02	.03	-.01	-.07*
CEN Component					
ICN 4	-.02	-.02	-.06	-.01	-.01
ICN 5	-.08**	-.03	.05	.00	-.03
ICN 6	.01	-.02	-.02	-.01	.02
ICN 7	-.03	.06	-.03	-.09**	.02
ICN8	-.02	-.03	.00	.00	.02

Notes. N = 985. * $p < .05$, ** $p < .01$. C = Conscientiousness, A = Agreeableness, N = Neuroticism, O = Openness/Intellect, E = Extraversion, GPN = goal priority network, CEN = central executive network, DN = default network

Lastly, I tested the specificity of associations between the GPN and Conscientiousness. I predicted that Conscientiousness would not be associated with the DN or the DAN. I computed partial correlations between Conscientiousness and ICNs in the DN and DAN controlling for sex, age, IQ, motion, and the other ICNs from the GPN, CEN, and either the DN or DAN respectively. DAN coherence was not significantly related to Conscientiousness; however, one of the eight DN ICNs (ICN 11, comprising the precuneus and the posterior cingulate cortex) was positively association with Conscientiousness (partial $r = .070$, $p = .029$). This effect remained significant when controlling for the other Big Five traits.

Interconnectivity and Conscientiousness. I also hypothesized that interconnectivity in the GPN during rest would be positively associated with Conscientiousness and that interconnectivity in the CEN during rest would not be associated with Conscientiousness. For these tests, I ran partial correlations controlling for age, sex, IQ, and motion. Because there were 3 GPN components, I calculated partial correlations for all three connections (ICN1vICN2, ICN1vICN3, and ICN2vICN3) and Conscientiousness. Two connections were related to Conscientiousness (ICN1-ICN3: partial $r = .075$, $p = .018$; ICN2-ICN3: partial $r = -.07$, $p =.037$). However, these results do not remain significant after controlling for the other Big Five traits (ICN1-ICN3: partial $r = .061$, $p = .054$; ICN2-ICN3: partial $r = -.048$, $p = .135$). See Table 2.3 on the next page for connectivity results.

I ran partial correlations to assess the relation between all ten CEN interconnections and Conscientiousness. Three CEN connections were significantly associated with Conscientiousness: ICN4-ICN5, ICN4-ICN7, and ICN5-ICN7 (see Table 2.3 for all tests). The connection between ICN4 and ICN5 was significantly associated with Conscientiousness (partial $r = -.088$, $p = .006$) after controlling for all other Big Five traits (partial $r = -.098$, $p = .005$), but is right at the threshold when accounting for multiple comparisons (p level would need to be .005 or less). The connection between

ICN 4 and ICN 7 is associated with Conscientiousness (partial r = .092, p = .004) and remains significant after correcting for multiple comparisons. This result also remains significant after controlling for the other Big Five (partial r = .075, p = .019). The connection between ICN5 and ICN 7 was associated with Conscientiousness (partial r = -.066, p = .040) but this result does not remain after controlling for the other Big Five traits (partial r = -.055 p = .088) and does not remain significant after accounting for multiple comparisons.

Table 2.3. *Partial correlations of the Big Five with GPN and CEN interconnectivity, controlling for age, sex, motion, and IQ.*

Connectivity	C	A	N	O	E
GPN Connectivity					
ICN1–ICN2	.04	.02	.02	-.05	-.01
ICN1–ICN3	.08*	.06*	-.04	-.04	-.01
1CN2–ICN3	-.07*	-.07*	.04	.05	.02
CEN Connectivity					
ICN4–ICN5	-.09**	-.06	.01	.02	-.01
ICN4–ICN6	-.05	-.05	-.02	.01	.07*
ICN4–ICN7	.09**	.05	-.06	-.02	.00
ICN4–ICN8	-.01	.02	-.02	.03	.05
ICN5–ICN6	.05	.07*	-.01	-.04	-.02
ICN5–ICN7	-.07*	-.05	.04	.05	.04
ICN5–ICN8	.01	-.04	-.05	-.05	.03
ICN6–ICN7	-.05	-.10**	.02	.03	.05
ICN6–ICN8	.00	-.03	-.03	-.04	.03
ICN7–ICN8	-.01	.02	.04	.05	-.01

Notes. N = 985. * $p < .05$, ** $p < .01$.

Connectivity and Externalizing:

Coherence and Externalizing. I hypothesized that individuals higher in externalizing behavior would have low levels of coherence and in the GPN and lower levels of coherence in the CEN (i.e. there would be a negative relation between externalizing behavior and connectivity in the GPN and CEN). To test these hypotheses, I ran partial correlations controlling for age, sex, IQ, motion, and the other ICNs that occupied similar regions. That is, I controlled for ICN coherence in the CEN, DN, and DAN when assessing the relation between the GPN and externalizing and I controlled for ICN coherence in the GPN, DN, and DAN when assessing the relation between CEN and externalizing.

There were no significant associations between GPN ICN coherence and any of the four externalizing measures (ASR rule breaking behavior, DSM ADHD problems, DSM inattention subscale, DSM hyperactivity-impulsivity subscale). See Table 2.4 for all tests. However, many relations were found between a component in the CEN (ICN 7) and three of the externalizing measures. Both the DSM inattention subscale and the DSM ADHD problem subscales were weakly negatively related to coherence in ICN7 (DSM inattention partial $r = -.074$, $p = .021$, DSM ADHD problems partial $r = -.065$, $p = .042$), but these results do not remain significant when accounting for multiple comparisons. The ASR rule breaking behavior showed a slightly stronger negative correlation with ICN7 (partial $r = -.152$, $p < .000$).

Lastly, I tested the specificity of associations with externalizing behavior. I predicted that externalizing would not be associated with the DN or the DAN. I computed partial correlations between externalizing measures and ICNs in the DN and DAN controlling for sex, age, IQ, motion, and the other ICNs from the GPN, CEN, and either the DN or DAN respectively. All DAN components showed relations between externalizing behavior and coherence; however, only one of these stays significant when accounting for multiple comparisons. ICN 7, comprising the superior parietal lobe and the lateral occipital cortex, was positively associated with ASR rule breaking (partial r = .112, p = .001). Of the eight DN ICNs, ICN 9 (which was visualized in the component selection section and included the DN structure and some parts of the VAN) was not associated with externalizing.

Table 2.4. *Partial correlations between externalizing measures and coherence of components in GPN and CEN, controlling for age, sex, IQ, motion, and components in DN, DAN, and either CEN or GPN.*

	ASR Rule Breaking	DSM ADHD	DSM Inattention	DSM Hyperactivity
GPN				
Component				
ICN 1	-.03	-.02	-.03	-.00
ICN 2	.00	.01	.01	.02
ICN 3	.00	.00	.04	-.05
CEN				
Component				
ICN 4	-.04	-.02	-.02	-.01
ICN 5	.02	.04	.05	.02
ICN 6	-.01	-.04	-.06	-.01
ICN 7	-.15**	-.07*	-.07*	-.04
ICN8	.02	-.01	-.02	-.01

Notes. N = 985. * $p < .05$, ** $p < .01$. GPN = goal priority network, CEN = central executive network, DN = default network

Interconnectivity and Externalizing. I also hypothesized that interconnectivity in the CEN and GPN during rest would be negatively associated with externalizing behavior. I ran partial correlations, controlling for age, sex, IQ, and motion, between all three GPN interconnections (ICN1vICN2, ICN1vICN3, and ICN2vICN3) and externalizing behavior. Two GPN connections were related to externalizing behavior. ASR Rule Following showed relations with ICN2-ICN3 connectivity (partial r = .081, p = .011) and also showed an association with the ICN1-ICN3 connectivity (partial r = -.065, p = .043) See Table 2.5 for connectivity results.

Table 2.5. *Partial correlations of externalizing behavior with GPN and CEN interconnectivity, controlling for age, sex, motion, and IQ.*

Connectivity	ASR Rule Breaking	DSM ADHD	DSM Inattention	DSM Hyperactivity
GPN Connectivity				
ICN1–ICN2	-.05	.03	.00	.06
ICN1–ICN3	-.07*	-.01	-.03	.02
1CN2–ICN3	.08*	.04	.05	.01
CEN Connectivity				
ICN4–ICN5	.10**	.08*	.06	.08**
ICN4–ICN6	.09**	.04	.03	.04
ICN4–ICN7	-.07*	-.10**	-.05	-.13**
ICN4–ICN8	.00	.02	.04	.00
ICN5–ICN6	-.08*	-.04	-.04	-.04
ICN5–ICN7	.02	.08*	.07*	.06
ICN5–ICN8	.00	-.04	-.04	-.03
ICN6–ICN7	.08*	.04	.03	.05
ICN6–ICN8	.04	-.03	-.05	.00
ICN7–ICN8	-.02	.02	.04	.00

Notes. N = 985. * p < .05, **p < .01.

I ran partial correlations to assess the relation between all ten connections in the CEN and externalizing behavior. Many CEN connections were significantly associated with externalizing behavior (see Table 5 for all tests and partial correlation coefficients). Of note, connectivity between ICN4 and the other CEN ICNs showed associations with externalizing behavior. Also, ICN4-ICN7 was significantly associated with most of the externalizing behavior measures used in the current study. The ICN5-ICN7 connection showed associations with externalizing behavior as well (DSM ADHD: partial $r = .077$, $p = .016$, DSM inattention: partial $r = .076$, $p = .017$).

Discussion

Even though Conscientiousness and externalizing behavior are related traits, their relations to functional connectivity have not previously been studied in the same sample. Supporting my hypothesis, connectivity and coherence in the CEN was negatively associated with externalizing behavior. However, my hypotheses about the GPN were not supported; neither Conscientiousness nor externalizing behavior showed associations with connectivity or coherence in the GPN (after accounting for multiple comparisons).

In the CEN, coherence in ICN 7, which was made up of the posterior cingulate cortex and the precuneus, was associated with attention problems, rule breaking, and general externalizing. That is, as coherence in this network decreases, externalizing behavior increases. Interestingly, connectivity between ICN7 and ICN4 (which contains the right paracingulate gyrus, posterior parietal cortex, frontal pole, supplementary motor area and middle temporal gyrus) decreased as externalizing behavior increased (DSM ADHD, DSM Hyperactivity). These externalizing measures were not significantly associated with ICN 7's coherence, but the relationship between these two CEN subnetworks is associated with externalizing and suggests that this connection may be reflective of general propensity for externalizing behavior as well as the hyperactivity parts of externalizing behavior. Results trended towards showing a positive relation between broad externalizing and hyperactivity and the ICN 7-ICN 5 connection (which shares some brain regions with the GPN). This may suggest that dissociation between the CEN and GPN is associated with more impulse control.

These data allowed me to run a post hoc analysis to investigate whether or not dissociation between the CEN and GPN would be associated with more impulse control. A post hoc analysis does suggest that hyperactivity is associated with increased connectivity between the GPN and CEN (ICN1-ICN5 partial $r = .084$, $p = .008$; ICN2-ICN4 partial $r = .085$, $p = .007$; ICN3-ICN8 partial $r = .086$, $p = .007$). This finding could inspire future research on ADHD in both adolescents and adults because most of the previous research on hyperactivity and inattention has focused on the lPFC. These findings suggest that there are other relevant brain areas and networks that would be worth investigating in the future.

Having such a large, publicly available dataset available is invaluable to novel research as well as those trying to replicate previous findings. However, using data that have been collected with novel protocols makes replication of previously published results more difficult. One potential limitation of the study is the way in which the data was acquired. Participants were asked to keep their eyes open, with a relaxed fixation on a bright crosshair on a dark background. Researchers who planned the protocol for the HCP argued that this method allowed them to gather a bigger range of spontaneously fluctuating modes of brain activity (Smith et al., 2013). However, this task may have been too minimal. That is, there were no checks to ensure that participants were fully awake during the scan and there were no checks to ensure that participants were truly engaging their mind in a “typical” resting manner. Previous research on functional connectivity has used minimal tasks wherein participants are asked to press a button when the fixation cross changes from white to gray or gray to white. This ensures that the participants remain awake, or that the researcher is able to identify when the participant fell asleep. It is possible that some participants in the current data set fell asleep or were creating different cognitive experiences for themselves, but there are no checks to control for such differences.

Interestingly, both Rueter et al. (2018) and the present analysis identified one component in the DN as being associated with Conscientiousness. In the current analysis, the DN component was included because it was comprised of regions found in both the DN and the GPN. ICN9 in the current sample included the dorsal prefrontal cortex and the inferior parietal lobe, but it also included the DN medial temporal lobe subsystem. Previous research has found that brain regions in the DN (and specifically the dorsal prefrontal cortex and the inferior parietal lobe) are more likely to change function from DN to attentional, control, or sensory networks (Betzel, Fukushima, He, Zuo, & Sporns, 2016). Additionally, the medial temporal lobe subsystem activates when people actively create mental images of their future self. In this way, the medial temporal lobe subsystem of the DN may be relevant to long-term goal maintenance, especially if it works in concert with regions in the GPN during rest.

The parameters of the resting state scans that were acquired for this project were different than the majority of resting state functional connectivity studies. HCP’s protocol reduced the TR from the typical 2 or 3 s to .72 ms, which increased the sensitivity of detecting functional connectivity fluctuation. The HCP protocol placed a higher priority on cortical, surface based analyses of fMRI data instead of a more “conventional 3d volumetric analysis” (S. M. Smith et al., 2013). While the reasoning for this choice makes sense (when conducting surface-based analyses, researchers reduce smoothing across distinct functional areas in pre-processing pipelines) it does bring into question whether or not researchers would be able to replicate volumetric based functional connectivity results. Lastly, HCP’s protocol also contained smaller the voxels than are typically used, which worsens the signal to noise ratio and the temporal resolution. Researchers on this project discuss that there is a loss of SNR due to the relatively high spatial resolution, but that this issue was dealt with by collecting an hour of resting state data from each subject. The length of this task, even when lumped into 15-minute sections, may encourage participants to spontaneously engage in more complex cognitive thoughts due to boredom or monotony.

Another limitation of the current study is the measurement of personality. The NEO-FFI is used frequently, but given the number of items for each trait, it is not the most rigorous way to assess personality. It is ideal to incorporate multiple informant reports because they provide unique information regarding an individual’s personality (Vazire, 2010). I may not have found associations with Conscientiousness because the NEO-FFI as a standalone measure is less reliable and less valid when measuring the true trait level of participants than studies with more extensive measures of personality. Both neural and personality measurements need to be reliable to discover replicable associations.

Lastly, there are a few limitations regarding the use of correlational studies and using functional connectivity components. Because the results from this study are correlational, inferences cannot be made about what causes the other. A positive association between coherence and a trait does not mean that the brain is causing the trait. Because functional connectivity can change with treatment or training, longitudinal studies of personality and functional connectivity may be able to investigate the causal nature of the relation in the future. One related limitation is that different ICNs were tested in this study compared to the original study by Rueter et. al (2018). The optimal way to replicate previous results would use the original components from Rueter et. al (2018) and to apply them to the resting state data using dual regression. Because the publicly available data was shared in CIFTI space (surface space and subcortical space combined into a single file) there was not a clear way to apply our previous components to the resting state data without reprocessing the raw data. Given the sheer volume of the data, limited storage abilities, as well as time constraints, this analysis was not completed.

Conclusion

This is the first study to investigate the neural networks that contribute to both Conscientiousness and impulsive externalizing. My results did not replicate previous findings that connectivity in the GPN is related to Conscientiousness (Rueter et al., 2018). However, some of my hypotheses were supported. Namely, functional connectivity across the CEN was associated with impulsive externalizing. Past research has focused on the lPFC as a major neural substrate of impulsivity or lack of inhibition (Aron, Robbins, & Poldrack, 2014; Ridderinkhof et al., 2004; Rueter, Abram, MacDonald, Rustichini, & DeYoung, 2018). The present analysis suggests that other parts of the CEN (e.g. the posterior cingulate cortex, the precuneus, the paracingulate gyrus, and posterior parietal cortex) may play equally important roles in inhibiting impulses. Resting state functional connectivity has been proposed as a more natural way to investigate how the brain functions in everyday life. Thus, it may be crucial to understand how all parts of the CEN and GPN interact to truly treat individuals who suffer from ADHD or high levels of impulsivity.

<u>Chapter 3:</u> Task-based Functional Networks and the Conscientiousness-Externalizing Spectrum

Introduction

While many functional connectivity studies have investigated neural networks at rest, few have investigated associations between traits and connectivity during tasks. The aim of the current investigation is to study how individual differences in goal achievement and self-control are related to functional connectivity in the brain while individuals complete a cognitive task. In the present study, I focus on the disinhibited externalizing spectrum by investigating both the high end (Conscientiousness) and the low end (impulsivity and disinhibition). By including both ends of the disinhibited externalizing spectrum in the same sample I hope to better understand neural systems that underlie both traits. Based on previous findings, the GPN and CEN are reasonable networks to propose as the neural correlates for Conscientiousness and the disinhibited externalizing spectrum (see Chapter 1 and Chapter 2). No previous studies have assessed how Conscientiousness and disinhibited externalizing behavior are associated with functional connectivity while completing a task.

Few studies have investigated how broad networks are organized spatially during task compared to rest. Broad networks (e.g. CEN, DN, GPN, and DAN) appear to occupy similar parts of the brain across a wide range of acquisition states (Krienen et al., 2014), but these networks reorganize spatially to some extent. Many researchers have found that the CEN, DN, GPN, and DAN occupy much of the frontal, temporal, and parietal lobes at rest (Yeo et al., 2011) and during cognitive tasks (Menon & Uddin, 2010). Krienen et al. (2014) found that these broad networks are located in generally the same position at rest as during tasks, but that the cortical locations and size of the networks differ slightly depending on the task that participants are completing in the scanner. Importantly, the dlPFC contains the CEN, DN, GPN, and DAN during rest and while completing tasks (Krienen et al., 2014; Yeo et al., 2011). When researchers placed a seed in the dlPFC to extract frontal networks across a variety of tasks, a single network emerged and showed similar activation across four different types of tasks that remained centrally located around the seed area (Krienen et al., 2014). However, the shape of coverage of this network changed slightly depending on the task that was being completed in the scanner.

When comparing resting state networks to networks extracted during task based studies, the following patterns have been identified by Krienan et al. (2014). During rest, the frontal cortex was made up predominantly of the GPN, DN, CEN, and DAN. During a counting task, the frontal cortex no longer contained the GPN, and rather the DAN took up much of the old GPN and DN area. During semantic tasks (including a word-based N-back), most of the frontal cortex showed associations with DAN and the GPN took over some of the somatomotor regions that were part of the DAN at rest. The CEN remained fairly stable across four different types of task (i.e., passive, count, semantic, and audio/visual) but appeared largest, spatially, during both rest and audio/visual tasks. The semantic task showed a laterality difference between the DAN and the CEN, where the CEN was large on the right frontal side of the brain and the DAN took up most of the left frontal region. Interestingly, their semantic tasks consisted of various, word-based, N-back tasks, with the addition of a task that simply played vocabulary words over and over again, meaning this may not be a pure representation of the networks during a semantic task (the N-back task is much more demanding than deciphering words). The DN remained fairly stable across the four tasks, but took up the most space during passive states, which is to be expected. During semantic tasks, the GPN took over regions of the anterior parietal lobe that shows associations with the DAN and the somatomotor network during rest. The GPN included regions in the dlPFC only during passive- or resting-states. These results suggest that cortical regions reconfigure spatially and that their connectivity patterns may also change in response to task demands (Shirer et al., 2012).

Task-based functional connectivity may not only impact the spatial organization of large-scale networks, it may also impact the timeseries of the networks. Using a novel method, Kucyi et al. (2017) studied dynamic fluctuations of functional connectivity of an fMRI scan and were able to compare fluctuations to isolated moment-to-moment behavior. Their study suggests that cognitive states are associated with different timeseries within the same network. Thus, spontaneous fluctuations in coherence (i.e., intranetwork connectivity) and internetwork connectivity reflect behavioral variability (e.g. behavior the participant is completing at a specific time; Krienen et al., 2014; Kucyi et al., 2017). To fully understand how the GPN and CEN are related to the disinhibited externalizing spectrum, we must study connectivity from many states (e.g. from both resting state and across different tasks) to be able to distinguish between stable network properties and contributions from networks that vary depending on the task at hand.

The present study examines the relation between disinhibited spectrum traits and functional connectivity during the multi-source interference task (MSIT, Bush & Shin, 2006). The MSIT can be thought of as a Stroop-like task because there are control and interference trials where an individual must inhibit a response that is more automatic in favor of the correct response. For example, on all trials, participants are asked to identify the number that is different than all the others. On the control trial, the number that is different is located at the button position that should be pressed (e.g. on a slide you see "100" and therefore, the 1 button should be pressed because the 1 is different). On interference trials, the number that is different is located at a different button position (e.g. on a slide you see "112" and therefore, the 2 button should be pressed because the 2 is different). Interference trials are more difficult because participants need to inhibit the impulse to press the 3 button (due to location of the target) and instead press the 2 button. Because of these Stroop-like properties that elicit prepotent responses that must be inhibited (Miyake et al., 2000), the MSIT is a reasonable task to investigate the relation between Conscientiousness, externalizing, and functional connectivity.

The MSIT was developed to be used to assess functional integrity of the dACC and dlPFC in patient populations but has also been validated in healthy controls (Bush & Shin, 2006). Previous studies have noted that accuracy on the MSIT should be high when administering the task to healthy adults (control trials: 99.4%, interference trials: 97.4%). The utility of the MSIT is that reaction times are much longer for interference trials than control trials, suggesting that interference trials are more difficult than control trials by requiring inhibition to correctly respond. Additionally, the MSIT is well validated in fMRI to activate the dACC, dlPFC, right insula, rIFG, and the superior parietal cortex (Bush, Shin, Holmes, Rosen, & Vogt, 2003; Deng, Wang, Wang, & Zhou, 2018). These brain regions also play roles in both the GPN and CEN, making this task useful for investigating the disinhibited externalizing spectrum.

Previous studies have used the MSIT to investigate the disinhibited externalizing spectrum more deeply. One study reported that 13-14 year olds with low behavioral ratings of inhibitory control had poorer performance on the MSIT as well as heightened activation in the PFC during interference trials (N = 157, Kim-Spoon et al., 2016). Based on these findings, individuals with higher levels of disinhibited externalizing likely experience heightened activation in the CEN and GPN while those with higher levels of Conscientiousness may experience lower activation in the CEN and GPN during interference trials.

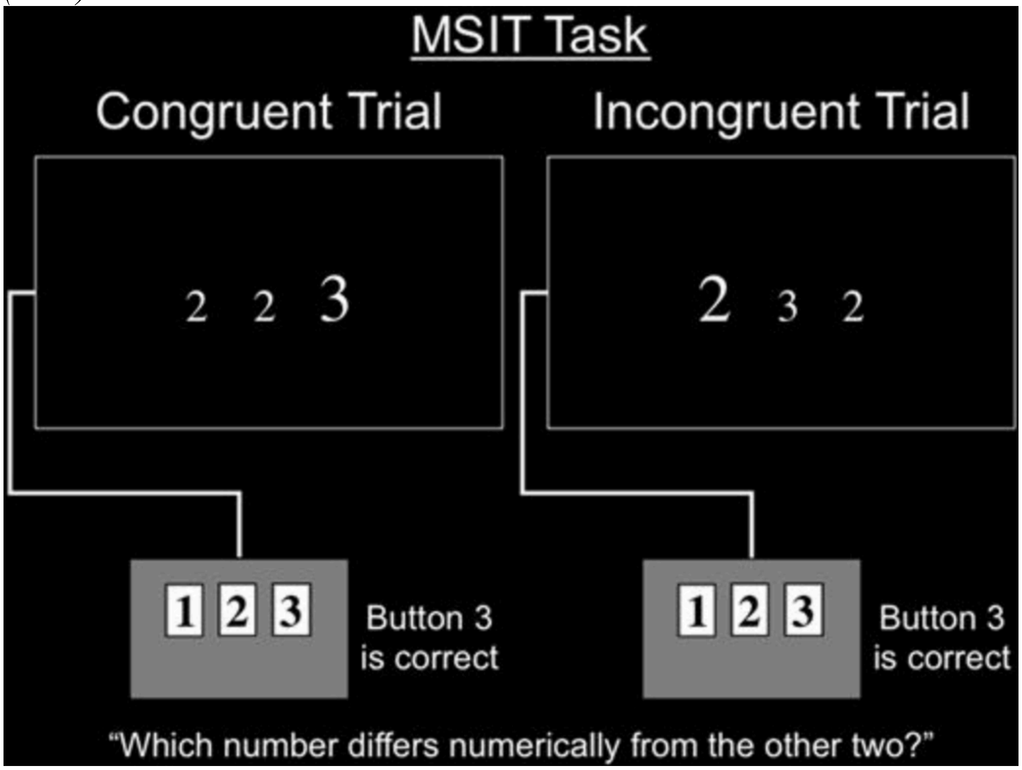
In this study, I examine the relation between the Conscientiousness-disinhibited externalizing spectrum and functional connectivity calculated from task-based data. The MSIT is a cognitive inhibition task, and thus, may elicit the traits of interest. It is important that healthy controls perform at or near ceiling on this task because it suggests that it is not highly demanding and reduces the extent to which intelligence is likely to be associated with functional connectivity during this task. Conscientiousness and intelligence are slightly negatively correlated (DeYoung, 2011; Duckworth, Peterson, Matthews, & Kelly, 2007), thus it is important for the present analysis that the MSIT elicit inhibition as opposed to intelligence or its closely related function, working memory. Individuals may complete the MSIT using varying cognitive strategies. Some individuals may complete the task in an enhanced way by paying closer attention to details and using self-discipline techniques (e.g. trying to increase their state inhibition by focusing harder to perform more efficiently). Others may be more likely to make impulsive decisions (because they were not able to inhibit a quick button press). Based on previous research, I predict that coherence and interconnectivity in the GPN will be positively associated with Conscientiousness and negatively associated with disinhibited externalizing behavior. I also predict that connectivity and coherence in the CEN will not be related to Conscientiousness but will be negatively related to disinhibited externalizing behavior. Disinhibited externalizing may be related to the CEN because the CEN covers much of the lPFC and is associated with IQ (Baddeley, 1996; Collette & Van der Linden, 2002; Tanji & Hoshi, 2008) and because disinhibited externalizing behavior and IQ are weakly negatively correlated (Andersson & Sommerfelt, 2001; Lynam, Moffitt, & Stouthamer-Loeber, 1993). However, Conscientiousness is likely unrelated to the CEN because Conscientiousness is generally unrelated to intelligence and working memory (DeYoung et al., 2009, 2011; Fleming, Heintzelman, & Bartholow, 2016).

Methods

Participants: The participants in this study (N = 114, all male, ages: 18 – 36, mean age: 22.95) were recruited through various Internet sites and via flyers from the community near New Haven, Connecticut. Roughly half of the sample consists of students (n = 60) from surrounding universities (including Yale and other nearby colleges). The other half of the sample consists of mostly lower- and middle-class individuals. Many individuals in this sample reported substance use and other externalizing behavior, suggesting the presence of adequate variance in the constructs of interest. Participants were given monetary compensation for their participation. One participant exhibited excess absolute head motion (greater than 1.3mm of absolute motion) during the scan and was consequently excluded from all processing pipelines in the present study because motion has been shown to cause spurious correlations between ICNs in functional connectivity analyses (Power, Barnes, Snyder, Schlagger, & Petersen, 2012). With alpha = .05, this sample (N = 113) has power of .83 to detect effect sizes of *r* = .27 or stronger. Additionally, ten subjects exhibited moderate head motion (greater than .5 mm of absolute motion) during the scan and were excluded from two of the analysis pipelines that did not correct for motion artifacts (e.g. using ICA-FIX).

Multi-Source Interference Task (MSIT): The MSIT was created to reliably activate the dACC and dlPFC (Bush & Shin, 2006). While completing this task individuals must abstain from responding to cognitive interference and correctly press buttons after being presented with a decision (Bush & Shin, 2006). Participants are presented with a row of three digits (ranging from 0 to 3) and asked to identify the one that differs from the other two, using buttons corresponding to 1, 2, and 3, in that order. Control trials have only 0s as distractors and target numbers are placed in the same position in the row as the correct response on the button box. Additionally, the target is larger in size than the distractors in the version of the MSIT used in the present study. Interference trials include distractors that are other potential targets (1, 2, or 3) and larger in size than the targets, and the target numbers are never placed in the same position as the correct key on the button box. The incongruence between location on the screen and the button one needs to press is analogous to a Stroop task (i.e. where one needs to state the color of the word instead of the word itself), but this task is more suitable than the original Stroop for completion in the scanner because verbal responses are not necessary. See Figure 3.1 on the next page for an example of both a congruent and incongruent MSIT trial.

Figure 3.1. *MSIT task example. As seen in Green, Kraemer, DeYoung, Fossella, & Gray (2013)*



Personality Questionnaires: All participants in the study completed the Big Five Inventory (BFI) and the Big Five Aspect Scales (BFAS). The BFI consists of 44 items that measure the Big Five personality traits (John, Naumann, & Soto, 2008) and the BFAS consists of 100 items (DeYoung et al., 2007). In the BFAS, there are 10 items measuring each of the two major subfactors or "aspects" of each of the Big Five traits. Sixty percent of the sample also has one or two peer ratings of the BFI (n = 68). When multiple peer ratings were available, they were averaged to create a single peer-rating score. The self-BFI and self-BFAS were averaged to create a composite Big Five self-score. Then the self- and peer- ratings of the Big Five were averaged and used as the final personality scores in this analysis.

Externalizing Behavior Measures: The two questionnaires that will be used as externalizing measures in this sample are a Hyperactivity/Impulsivity ADHD symptoms (adult) questionnaire and the UPPS Impulsivity Scales (Whiteside, Lynam, Miller, & Reynolds, 2005). Both of these questionnaires were administered within a laboratory setting at Yale University.

The UPPS Impulsivity Scales measure four primary types of impulsivity which include urgency, lack of premeditation, lack of perseverance, and sensation seeking (Whiteside et al., 2005). Urgency is the tendency to experience strong impulses, sometimes under influences of negative affect. Lack of premeditation reflects the lack of the tendency to think through the consequences of an action before completing the action. Lack of perseverance is often related to being unable to focus on boring or difficult tasks, and lastly, sensation seeking reflects a willingness to engage in risk-taking behaviors for the sake of excitement. For this measure, sixty percent of subjects have both self- and peer- ratings for the following scales: sensation seeking, lack of premeditation, and urgency (n = 68). The items used in the lack of perseverance sub-scale are framed in a way that would make the trait hard to observe by informants. Thus, it was not administered in the peer-rating packets. When multiple peer ratings were collected, they were averaged to create a single peer-rating score. When peer ratings were not available, self-ratings were used in the analysis. See Appendix 1 for the items in this questionnaire.

To assess hyperactivity and impulsivity symptoms, DSM-IV ADHD symptoms were self-rated both retrospectively prior to the age of 7 and also after the age of 7 and into adulthood. See Appendix 3 for the items that were administered.

Because I am interested in a broad measure of disinhibited externalizing, I averaged some of the externalizing measures listed above to create a single index of disinhibited externalizing. I did not include UPPS Sensation seeking or UPPS Urgency in the main index. UPPS Sensation Seeking was not associated with Conscientiousness and UPPS Urgency was more strongly associated with Agreeableness, suggesting that these scales may reflect different constructs than disinhibited externalizing. To create a single index, I standardized the following measures and averaged them: lack of premeditation, lack of perseverance, ADHD inattention, ADHD impulsivity/hyperactivity. This single index is the main measure used to test hypotheses in the present study.

Intelligence: Participants in this study completed four subtests of the Wechsler Adult Intelligence Scale – Third Edition (WAIS-III) including block design, matrix reasoning, vocabulary, and similarities (Wechsler, 1997). These subtests can be used to estimate participants' full scale IQ using the WAIS manual. IQ is included as a covariate because of its weak negative relation with Conscientiousness and its relation with resting state connectivity (Cole et al., 2012; Song et al., 2008; Wang et al., 2011).

Image Acquisition & Preprocessing: Functional MRI scans were acquired at Yale University while participants completed the MSIT task in a 3T Allegra MRI scanner (Siemens, Erlangen, Germany). Parameters of the scan sequence included: gradient-echo echo planar imaging of 183 volumes; repetition time (TR) = 2 s; echo time (TE) = 25 ms; FOV = 256 mm; flip angle = 80°; voxel size = 3.75 x 3.75 x 4 mm. Additionally, a high resolution T1-weighted MPRAGE image was collected for registration during pre-processing.

Pre-processing steps were completed using the FMRIB Software Library (FSL 5.0.9) and included the following steps: brain extraction to mask out non-brain voxels, correcting for head motion and distortion (B0 distortion), high-pass temporal filtering (at a filtering threshold of 0.1 Hz), registering the timeseries to the structural data and resampling the EPI sequences into standard space (2mm MNI space). I then utilized three different processing pipelines to see which resulted in the cleanest components. The three processing pipelines can be described as follows: (1) a meta-ICA pipeline conducted on non-fixed data with more stringent absolute motion criteria, (2) a meta-ICA pipeline conducted on fixed (i.e. cleaned) fMRI data with less stringent absolute motion criteria, and (3) ICNs from a meta-ICA previously conducted in a larger sample (N =218, see Rueter et al., 2018 for more information on this sample) were dual-regressed onto the non-fixed data. Ten subjects used in pipeline 2 were not used in pipelines 1 or 3 because previous research has shown that head motion in functional connectivity studies can cause artifacts that create spurious correlation patterns between ICNs (Power, Barnes, Snyder, Schlagger, & Petersen, 2012) and because those pipelines did not use ICA-FIX to clean the data. For that reason, I excluded participants with absolute movement greater than .5 mm in the pipelines that did not include ICA-FIX as a preprocessing step.

For the first pipeline, I ran twenty-five group-level, probabilistic, spatial ICAs using MELODIC (Multivariate Exploratory Linear Optimized Decomposition into Independent Components) in FSL (https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/MELODIC). Each of these runs included a randomly generated order of all participants as inputs, which reduced any order effects that could have biased the resulting functional connectivity values. I extracted 50 components because dimensionalities around 40 or 50 are most reproducible (Poppe et al., 2013). These 50 components from each meta-ICA were temporally concatenated into a single file and were then used as the input to a meta-level MELODIC analysis to derive the 50 most consistent group-level components. The nonartifactual components were normalized and then thresholded at a $z_{max} > 0.30$. I then applied these group level components to the subject level data using dual regression to obtain spatial maps and timeseries that correspond to each map for each individual. This pipeline was run on non-fixed data. Pipeline two was identical to the first, except I ran FSL's ICA FIX on the data to autoclassify components as "good" or "bad" to remove the bad components from the subject level 4D data (Griffanti et al., 2016; Salimi-Khorshidi et al., 2014). For pipeline three, I used the same pre-processed data as in pipeline one and applied a set of masks for 60 components from a previous, larger sample to the current sample using dual regression (see Rueter et al., 2018).

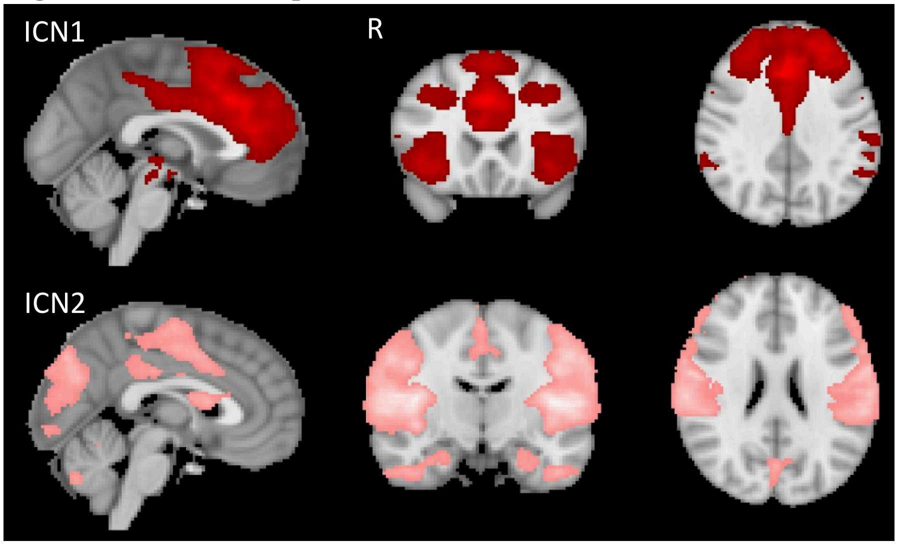
I used the set of connectivity metrics derived from pipeline three for the following reasons: (1) the ICNs from pipeline three were more clear and had fewer noisy artifacts, (2) the maps used in pipeline three were derived from a sample about twice as large as the current sample and, thus, are likely to be more reliable, and (3) the task data had a lot of mechanical noise, which created many "noise" components in pipeline one and pipeline two (ICA FIX set on the most stringent of the recommended parameter range was not able to adequately clean the data to create fewer artifacts). It is likely this is a limitation of the fMRI data used in the present analysis.

Functional Connectivity Metrics: Connectivity within each ICN (coherence) was computed as the average of individual correlations between every voxel within an ICN with the mean time-series for all voxels in that ICN. This step is done on the subject level by using subject-specific spatial maps that are derived via dual regression. Interconnectivity, or how much one component correlates temporally with another component, was computed as the Fisher z-transformed correlation between the mean time series of each ICN pair for each subject by using the subject-specific timeseries derived from dual regression.

Component Selection: Components can change shape slightly from resting state scans to task data; thus, three methods were used to classify and select networks in the present analysis. Thresholded group probability maps were visually inspected to identify artifactual components following procedures outlined by previous research (Kelly et al., 2010). These methods included identifying artifacts that reflect cardiac function, breathing, nonneural fluctuations or mechanical noise, white matter tracts, and movement.

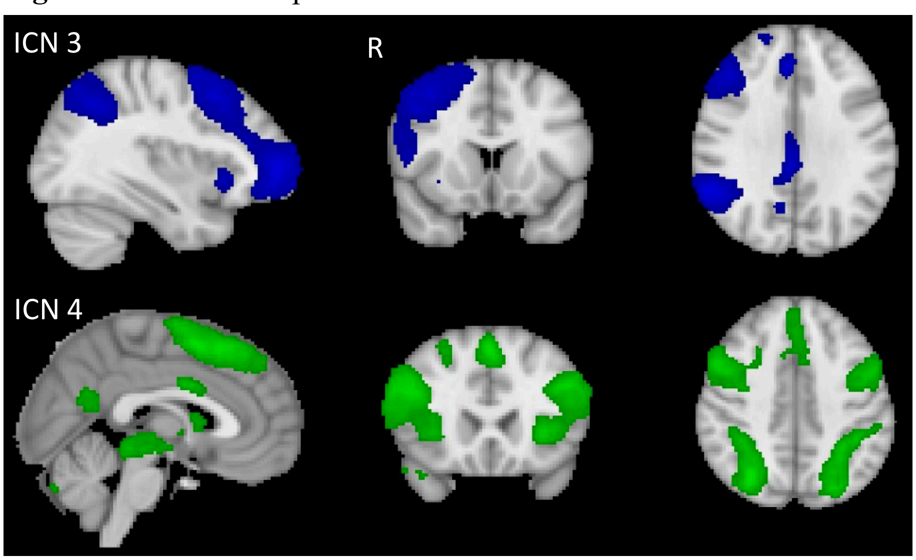
Then I calculated percentage of cortical overlap of each component with the parcellations for GPN, CEN, DN, and DAN as identified by Yeo et al. (2011) to identify which components corresponded most closely to each network. I visually inspected components with the highest overlap with each network to confirm that their clusters were centered on the proposed network. The set of 60 components has two components that reflect the GPN (ICNs 1 – 2), two components that reflect the CEN (ICNs 3 - 4), three components that reflect the DN (ICNs 5 – 7), and two components that distinctly reflect the DAN (ICNs 8 - 9). I am most interested in the networks that are central to our hypotheses, the GPN and CEN. Within the GPN, ICN 1 includes regions of the anterior cingulate cortex (ACC), temporal operculum, posterior cingulate cortex, dlPFC, and insula. ICN 2 includes core regions from the salience network including; the ACC and insula. ICN 2 also includes the operculum cortex, dlPFC, bilateral hippocampi, and frontal poles. See Figure 3.2 (next page) for visualizations of the GPN components.

Figure 3.2. GPN Components.



Within the CEN, ICN 3 is comprised of the lPFC, inferior frontal gyrus, frontal pole, superior parietal lobe, precuneus, and superior frontal gyrus. ICN 4 includes the superior frontal gyrus, insula, inferior frontal gyrus, lPFC, superior parietal lobe, precuneus, and the lateral occipital lobe. See Figure 3.3 (below) for visualizations of the CEN components. The remaining networks in the DN and DAN are not explained in detail because the DN and DAN networks will be used only in the partial correlation analyses as control variables.

Figure 2.3. CEN Components.



Motion parameters: I included a motion parameter that quantifies head motion during the fMRI scan because motion can cause spurious correlations between intrinsic connectivity networks that are extracted using ICA (Power et al., 2012). Absolute root-mean-squared (RMS) movement was included as the index of motion. Absolute RMS is a summary statistic that reflects the average movement across translational displacement across X, Y, and Z axes as well as rotational displacements across pitch, yaw, and roll.

Results

See Table 3.1 (next page) for descriptives and zero-order correlations for the behavioral variables in the current study.

Connectivity and Conscientiousness:

Coherence & Conscientiousness: I hypothesized that coherence in the GPN during the MSIT task would be associated with Conscientiousness and that coherence in the CEN during the MSIT task would not be associated with Conscientiousness. To test these hypotheses, I ran partial correlations controlling for age, IQ, motion, and other ICNs that occupy similar regions as the GPN and CEN. When testing associations between the GPN and Conscientiousness, I controlled for coherence in the CEN, DN, and DAN. When testing associations between the CEN and Conscientiousness, I controlled for coherence in the GPN, DN, and DAN. See Table 3.2 for all tests.

In line with my hypotheses, coherence in one of the GPN ICNs (ICN 2, comprising the ACC, operculum cortex, dlPFC, bilateral hippocampi, insula, and frontal poles) was significantly associated with Conscientiousness (partial $r = .29$, $p = .004$). This became an even stronger effect when controlling for the other Big Five traits (partial $r = .34$, $p = .001$). This effect remains significant after Bonferroni correction for multiple

Table 3.1. *Descriptives and zero-order correlations among behavioral variables.*

Variables	C	A	N	O	E	IQ	U-SS	U-Pre	U-Per	U-Urg	H-I	Inatt	EXT
Conscientiousness	-												
Agreeableness	.21	-											
Neuroticism	-.30	-.36	-										
Openness	-.05	.14	-.11	-									
Extraversion	.13	.16	-.39	.18	-								
IQ	-.05	.11	-.17	.24	-.01	-							
UPPS – Sensation Seeking	.01	.02	-.23	.25	.31	.04	-						
UPPS – Lack of Premed	-.48	-.19	-.10	.03	.23	-.09	.27	-					
UPPS – Lack of Perseverance	-.78	-.22	.35	-.05	-.26	.04	-.13	.33	-				
UPPS – Urgency	-.39	-.42	.57	-.08	-.03	-.18	-.01	.26	.31	-			
ADHD – Hyper- Impuls	-.27	-.20	.31	-.11	.02	-.08	-.03	.16	.24	.32	-		
ADHD – Inattention	-.62	-.20	.37	-.13	-.21	-.06	-.16	.22	.59	.37	.57	-	
EXT	-.81	-.28	.33	-.01	.02	-.03	.09	.62	.78	.42	.66	.80	-
Mean	-.01	.00	.01	.00	.01	121.9	.02	.02	2.44	.02	4.87	4.87	
SD	0.87	.84	.86	.88	.87	11.7	.94	.91	.73	.91	3.14	3.54	

Notes. N = 103. All correlations greater than .127 in absolute value are significant at $p< .0$

test. No CEN ICNs showed associations with Conscientiousness, which is also in line with my hypotheses.

To test for specificity, I ran partial correlations between the other Big Five traits and the GPN networks of interest to investigate whether or not Conscientiousness is specifically associated with this GPN network. Extraversion (a trait reflecting enthusiasm, approach behavior, and sociability) was associated with both GPN ICNs (ICN 1, partial $r = .24$, $p = .024$; ICN 2, partial $r = .23$, p = .031). However, after controlling for the other Big Five traits, the association with ICN 1 was no longer significant but the association between Extraversion and ICN 2 remained so (partial $r = .23$, $p = .035$). However, this association did not hold after correcting for multiple comparisons.

Table 3.2. *Partial correlations between the Big Five and coherence of components in GPN and CEN, controlling for age, sex, IQ, motion, and components in DN, DAN, and either CEN or GPN.*

	C	A	N	O	E
GPN Component					
ICN 1	.08	.16	-.16	.03	.24*
ICN 2	.29**	.03	-.11	.17	.23*
CEN Component					
ICN 3	-.04	-.02	-.05	-.13	-.13
ICN 4	.01	.01	.03	.14	-.02

Notes. N = 103. * $p < .05$, ** $p < .01$. C = Conscientiousness, A = Agreeableness, N = Neuroticism, O = Openness/Intellect, E = Extraversion, GPN = goal priority network, CEN = central executive network, DN = default network

To ensure that the relation between the GPN and Conscientiousness was specific to the GPN, I also ran partial correlations between the DN and DAN and Conscientiousness. Similar to the previous analyses, I computed partial correlations between Conscientiousness and ICNs in the DN and DAN controlling for sex, age, IQ, motion, and the other ICNs from the GPN, CEN, and either the DN or DAN, respectively. Coherence in DAN ICNs was not significantly related to Conscientiousness. One of the three DN ICNs comprising the dorsal medial prefrontal cortex subsystem of the DN (Andrews-Hanna, Reidler, Sepulcre, Poulin, & Buckner, 2010) was negatively associated with Conscientiousness (partial r = -.26, p = .012). This association stays significant even when controlling for the other Big Five traits (partial r = -.25, p = .019) and holds after correcting for multiple comparisons.

Interconnectivity & Conscientiousness: I hypothesized that interconnectivity in the GPN would be related to Conscientiousness and that interconnectivity in the CEN would not be related to Conscientiousness. To test my hypotheses, I ran partial correlations between interconnectivity values in the GPN and CEN and Conscientiousness controlling for age, IQ, and motion (sex was not a covariate because the entire sample is male). Because coherence in one of the GPN ICNs was associated with Conscientiousness, I would expect to see associations between connectivity in the GPN and Conscientiousness.

There were two GPN ICNs in this study. Thus, I calculated partial correlations between the only connection in the GPN (ICN1vICN2) and Conscientiousness. GPN connectivity was not associated with Conscientiousness (ICN1-ICN2 partial r = .095, p = .346); however, CEN connectivity was associated with Conscientiousness (ICN3-ICN4 partial r = .201, p = .045). When controlling for the other Big Five, the CEN result no longer remains significant (partial r = .166, p = .106). Neuroticism showed associations with GPN connectivity (partial r = -.22, p = .030) but this does not hold when controlling for the other Big Five traits (partial r = -.19, p = .062). I also examined whether or not connectivity between these networks was associated with Conscientiousness. No connections between the GPN and CEN were significantly associated with Conscientiousness. See Table 3.3 below for all connectivity results.

Table 3.3. *Partial correlations of the Big Five with GPN and CEN interconnectivity, controlling for age, sex, motion, and IQ.*

Connectivity	C	A	N	O	E
GPN Connectivity					
ICN1–ICN2	.10	.15	-.22*	.18	.04
CEN Connectivity					
ICN3–ICN4	.20*	.00	-.19	-.04	.12
GPN-CEN Connectivity					
ICN1–ICN3	-.03	-.16	.05	.12	.11
ICN1 – ICN4	-.04	-.07	-.12	.26**	.06
ICN2–ICN3	.08	-.03	-.01	.10	.04
ICN2–ICN4	.04	-.09	-.05	.10	-.05

Notes. N = 103. * $p < .05$, ** $p < .01$.

Connectivity and Externalizing:

Coherence & Externalizing: I hypothesized that the main index of externalizing behavior would be negatively associated with coherence in the GPN and negatively associated with coherence in the CEN. To test these hypotheses, I ran partial correlations controlling for age, IQ, motion, and the other ICNs that occupy similar regions as the GPN and CEN (i.e. DN, DAN, and either the GPN or CEN depending on the analysis.)

No components in the GPN or CEN were associated with the broad index of disinhibited externalizing. Therefore, I also conducted exploratory analyses to investigate associations between the GPN and specific externalizing subscales. ICN 2 was negatively associated with UPPS lack of perseverance (partial r = -.289, p = .005). ICN 1 was positively associated with UPPS sensation seeking (partial r = .246, p = .018). Coherence in ICN 3 was negatively associated with UPPS Sensation Seeking (partial r = -.23, p = .027). When controlling for the other UPPS traits, this effect becomes even stronger (partial r = -.288, p = .006). See all tests in table 3.4 below.

Table 3.4. *Partial correlations between externalizing measures and coherence of components in GPN and CEN, controlling for age, sex, IQ, motion, and components in DN, DAN, and either CEN or GPN.*

	EXT	UPPS Urgency	UPPS Sens Seek	UPPS Lack of Premed	UPPS Lack of Pers	Adult ADHD – Hyp Impuls	Adult ADHD – Inattention
GPN							
Component							
ICN 1	.05	.02	.25*	.15	-.08	.12	-.01
ICN 2	-.14	.02	.12	-.08	-.29**	.12	-.14
CEN							
Component							
ICN 3	-.02	.02	-.23*	.10	-.08	-.10	-.01
ICN 4	-.03	-.14	-.13	-.11	-.05	.01	.02

Notes. N = 103. * $p < .05$, ** $p < .01$. GPN = goal priority network, CEN = central executive network

To test the specificity of these exploratory associations between the GPN and CEN and externalizing behavior, I computed partial correlations between externalizing measures and ICNs in the DN and DAN controlling for sex, age, IQ, motion, and coherence in the GPN, CEN, and DAN or DN, respectively. One DAN component (comprising the postcentral gyrus, superior parietal lobe, angular gyrus, and central opercular cortex) was associated with ADHD hyperactivity impulsivity (partial r = -.220, p = .035); however, this does not remain significant after correcting for multiple tests.

Coherence in one of the DN components (the same DN component that was associated with Conscientiousness, comprising the dorsal medial prefrontal cortex subsystem of the DN) was positively associated with UPPS Lack of Perseverance (partial $r = .220$, $p = .034$).

Interconnectivity and Externalizing. I hypothesized that interconnectivity within and between the CEN and GPN during a task would be negatively associated with externalizing behavior. To assess this, I ran partial correlations to assess the relation between connectivity in the CEN, GPN, and between the two networks and externalizing behavior while controlling for age, IQ, and motion. The broad index of externalizing was not associated with interconnectivity in or between the CEN and GPN. I also conducted exploratory tests of the subscales of disinhibited externalizing to test if connectivity in or between the CEN and GPN was associated with specific facets of externalizing. GPN connectivity was associated with UPPS sensation seeking (partial $r = .359$, $p < .000$). Connectivity between the CEN and GPN components was significantly associated with UPPS Sensation seeking as well. See all interconnectivity results in Table 3.5 (next page).

Discussion

Conscientiousness and externalizing behavior are related traits, but their relation to functional connectivity has not previously been studied by investigating task-based functional connectivity in the same sample. This is the first study investigating the relation between functional connectivity derived from task-based data and these two traits of interest. I had two hypotheses for the current study: (1) connectivity and coherence in the GPN (and not the CEN) will be associated with Conscientiousness, and (2) connectivity and coherence in both the GPN and CEN will be associated with externalizing behavior.

Table 3.5. *Partial correlations of externalizing behavior with GPN and CEN interconnectivity, controlling for age, sex, motion, and IQ.*

	EXT	UPPS Urg	UPPS SS	UPPS L Premed	UPPS L Pers	Adult ADHD Hyp Imp	Adult ADHD Inatt
GPN Connectivity							
ICN1–ICN2	.02	-.05	.36**	.16	-.03	-.02	-.05
CEN Connectivity							
ICN3–ICN4	-.13	-.16	.15	-.11	-.10	-.12	.-08
GPN-CEN Connectivity							
ICN1–ICN3	.11	.18	.26*	.09	.05	.12	.07
ICN1–ICN4	.16	.15	.35**	.21*	.10	.07	.09
ICN2–ICN3	-.01	.14	.20*	.05	-.03	-.05	.01
ICN2–ICN4	.06	.13	.12	.10	-.02	.00	.11

Notes. N = 103. * $p < .05$, **$p < .01$.

Supporting my hypotheses and replicating previous findings (Rueter et al., 2018), Conscientiousness was positively associated with coherence in the GPN. More specifically, a network containing the ACC, dlPFC, insula, frontal pole, and bilateral hippocampi was positively associated with Conscientiousness. As Conscientiousness scores increased, connectivity within this network increased as well. Much of this specific component visually looks like the salience network, which integrates external stimuli to assess whether or not emotions or motivations are important to one's goals (Fox et al., 2006; Seeley et al., 2007; Uddin, 2015). However, there are some additional brain regions in ICN 2 that are not found in what has traditionally been labeled as the salience network, most notably in dlPFC, and this may be crucial for the link to Conscientiousness.

It is likely that the VAN and salience network work together to assist in goal prioritization. The VAN helps individuals ignore distractions and the salience network helps coordinate sensory and motivational information relevant to one's long term goals(Fox et al., 2006; Uddin, 2015). Importantly, connectivity between this network and another network in the GPN (comprising the ACC and a larger portion of the lPFC) was not associated with Conscientiousness, which suggests that intranetwork communication in a specific network is potentially more important for Conscientiousness rather than internetwork communication. Conscientiousness was not associated with coherence or interconnectivity in the CEN (after accounting for multiple comparisons), in keeping with my hypotheses.

Externalizing traits also showed associations with functional connectivity. UPPS lack of perseverance was significantly negatively associated with ICN 2, the same ICN that was associated with Conscientiousness. This is not surprising because this particular measure is strongly, negatively, correlated with Conscientiousness ($r = -.784$, $p < .000$ in the current sample). However, this finding is important because it suggests that the GPN may be associated with both successful life outcomes and maladaptive behavior, such as being unable to focus on boring or difficult tasks.

Sensation seeking was moderately positively associated with coherence in the GPN and moderately negatively associated with coherence in the CEN. Sensation seeking also showed a moderate positive relation with connectivity in the GPN and with connectivity between the CEN and GPN. That is, the higher the connectivity between

GPN ICNs and also between CEN and GPN ICNs, the higher an individual scored on sensation seeking, which reflects one's likelihood of engaging in risk-taking to enhance their excitement. In this sample, Conscientiousness was not significantly associated with UPPS Sensation seeking (r = -.02, p = .868). This finding is in line with previous research on the relation between the different UPPS subfactors. Whiteside & Lynam (2001) reported the intercorrelations between the UPPS subscales. UPPS Sensation Seeking was only slightly correlated with the other subscales and appears to mostly reflect dangerous risk-taking. These findings may seem contradictory as GPN connectivity is positively associated with Conscientiousness. However, previous research suggests that two cognitive mechanisms are present in sensation seeking: strong approach behavior and weak avoidance responses (Collins et al., 2012). It is possible that connectivity in the GPN is related to the approach-oriented behavior and less with the weak avoidance responses. Another network of the brain may contribute to weak avoidance responses.

One interesting finding was that a network in the DN was associated with both Conscientiousness and UPPS Lack of Perseverance. As previously discussed, these two measures are similar in nature (Lack of Perseverance is very similar to Industriousness, an aspect of Conscientiousness). This particular DN component most closely aligns with the dorsal medial prefrontal cortex subsystem of the DN, but why would this network in the brain be associated with Conscientiousness and Lack of Perseverance? First, the brain regions implicated in this subsystem are similar to some of the regions we see involved in the GPN. Also, this network, comprising regions in the TPJ and the dorsomedial PFC, is historically a subsystem of the DN that is associated with mentalizing, a cognitive process whereby individuals are able to reflect and infer the mental states of others and the self (Andrews-Hanna, Reidler, Sepulcre, Poulin, & Buckner, 2010). Perhaps successfully achieving one's long term goals is, indeed, associated with reflecting on the mental state of the self. Second, the DN is the most likely network to join the CEN, GPN, or DAN depending on the task being completed in the scanner (Betzel, Fukushima, He, Zuo, & Sporns, 2016). Thus, because ICNs were classified using Yeo et al.'s (2011) components from participants at rest, our classifications of networks from the MSIT task may contain some error. It may have been recruited as an attentional network given the cognitive demands on participants while completing the MSIT task.

There are some limitations to the current study. The first is that the sample consists only of males, which limits the generalizability of the current findings. However, given the findings replicated previous results from a larger, resting state sample, it adds value to the literature by being the first study assessing relations between task-based functional connectivity data and personality traits that may be elicited by the task. The second limitation is sample size. While a sample of 103 is not small by typical standards in neuroimaging, it's not as large as some of the more recent resting state functional connectivity studies and does not have high power (.65) to detect effects the size of those in our previous study (partial r = .22, Rueter et al., 2018). Additionally, when conducting ICA on task-based data, we noticed that the networks were less clean and did not appear to follow the typical broad neural networks as cleanly as previous work. Thus, we used components derived from a larger sample in our dual regression stage. In the future, it would be ideal to run ICA using task data on a larger sample.

Conclusion

This study is the first task-based functional connectivity study to investigate how Conscientiousness and disinhibited externalizing are related to broad neural networks. Our results indicate that Conscientiousness and lack of perseverance, a related externalizing trait, are both associated with coherence in a subnetwork of the GPN. This subnetwork comprises the traditional salience network in addition to the dlPFC and frontal pole. While sensation seeking may not precisely reflect disinhibited externalizing, its relation with GPN and CEN connectivity is important when considering the role these networks play within the externalizing domain. Resisting impulses and orienting oneself towards goals are both important behaviors implicated in successfully navigating life. Further research on these networks, their connectivity, and how they change depending on task demands may help us create therapies to increase Conscientiousness and reduce self-compromising, maladaptive, components of externalizing behavior.

Chapter 4: General Discussion & Conclusions

No studies have assessed the relation between both Conscientiousness and disinhibited externalizing and functional connectivity in the brain in the same sample. Moreover, many of the previous studies that assessed the relation between externalizing behavior and functional connectivity were conducted on children or adults with ADHD diagnoses compared with controls. These types of studies dichotomize groups while traits are normally distributed. When investigating neurobiological correlates of personality, it is important to assess individuals in the normal population if we hope to be able to generalize our results to the entire population. This dissertation is the first study to investigate traits that emphasize both the high and low ranges of the Conscientiousness-disinhibited externalizing spectrum in relation to functional connectivity.

After conducting ICAs in both resting state (Study 1) and task-based fMRI data (Study 2), I was able to conceptually replicate previous findings by Rueter et al. (2018) in Study 2, but not in Study 1. In Study 2, coherence in a network comprised of an extended salience network (that included the typical salience network and dlPFC) was positively associated with Conscientiousness. I was also able to extend these findings by investigating measures of disinhibited externalizing. Finally, this study also investigated whether or not connectivity computed from a task that elicits cognitive control was associated with the traits of interest, as opposed to relying on connectivity at rest. Some broad findings are explained in further detail below.

Conscientiousness is likely associated with the GPN. As reviewed in Chapter 1, previous research suggests that structure and function in brain areas found in the GPN are associated with Conscientiousness and similar behavior. In Study 2 (Chapter 3), a GPN component was associated with Conscientiousness and was similar in size and shape to the component identified by Rueter et al. (2018). It is important to note that the same ICNs from Rueter et al. (2018) were dual regressed onto the MSIT data in Study 2. Thus, we would expect to see similar components and associations if the association with Conscientiousness was able to be generalized from resting state to task data. Dual regression does allow the original ICNs to change in size and shape, but the Study 2 component, like that identified by Rueter et al. (2018), closely maps onto the salience network but with some additional areas of the brain including the dlPFC and the frontal poles. This component is closely approximated by the broad salience network identified in Yeo et al's (2011) 17-network parcellation as well. This fine grained parcellation splits the broad neural networks into smaller subnetworks.

In contrast to Study 2, Study 1 (Chapter 2) did not replicate the association of a GPN network with Conscientiousness. There are several reasons that Study 2 may have found associations where Study 1 did not, despite the fact that Study 2 (N = 103) had one tenth the number of subjects as Study 1 (N = 985). Study 2 had limitations (only male subjects, mechanical noise in the fMRI data) but it also had several strengths. One of those strengths is that it had robust personality measures in the form of both self- and peer-reports, allowing for more accurate assessment of personality traits. Additionally, Study 2 incorporated two different measures of the Big Five , which increases reliability of the personality measures. Study 1 had extensive neuroimaging data available, but it was collected using novel methodologies. It is uncertain whether or not these new methods would allow for replicability of typical functional connectivity results. In addition to new neuroimaging methods, Study 1 utilized data that had a much shorter measure of personality and only had self-report data available. These personality data are unlikely to be as reliable as the measures from Study 2, which could contribute to our lack of findings in this sample.

Subscales of externalizing appear to be associated with the GPN and CEN, but general disinhibited externalizing only showed associations with the CEN. Previous research suggests that dysfunction related to ADHD is related to frontostriatal circuitry, including the lPFC, dACC and striatum (Bush, Valera, & Seidman, 2005). Connectivity in the insula is associated with general disinhibition and substance use (Abram et al., 2015). These findings all include regions in the brain that are found in the CEN. In the present studies, general indices of disinhibited externalizing were not associated with the GPN. However, the general index of externalizing in Study 1 was associated with connectivity in the CEN (see Table 4.1 below for a summary of all associations from both Study 1 and Study 2). Exploratory analyses revealed that sensation seeking showed positive associations with the GPN. It is important to note that UPPS Sensation Seeking has been classified empirically as a facet of Extraversion and not a facet of Conscientiousness, and the two behavioral aspects of sensation seeking are approach behavior and weak avoidance responses (Collins et al., 2012; Whiteside & Lynam, 2001). Thus, connectivity in the GPN may also be related to approach-oriented behavior.

Coherence in CEN networks was negatively associated with many different measures of disinhibited externalizing, which is in line with my hypotheses and previous research. However, interconnectivity between CEN networks was mostly positively associated with externalizing behavior. This may suggest that overconnected CEN networks are detrimental to goal-oriented behavior and focusing on cognitive tasks. More research will be necessary to disentangle why interconnectivity in CEN networks would be positively associated with disinhibited externalizing but that coherence within CEN networks would be negatively associated with disinhibited externalizing. Additionally, the fact that these positive associations were found in only one of two studies suggests they might be false positives.

Table 4.1. Associations between disinhibited externalizing and GPN and CEN functional connectivity.

Externalizing Measure (Study)	**GPN Coherence**	**GPN Connectivity**	**CEN Coherence**	**CEN Connectivity**
ASR Rule Breaking (1)			-	+
DSM ADHD* (1)				-
DSM Hyperactivity (1+2)				+/-
DSM Inattention (1+2)				
Disinhibited Externalizing* (2)				
UPPS Sensation Seeking (2)	+	+	-	
UPPS Lack of Perseverance (2)	-			
UPPS Lack of Premeditation (2)				
UPPS Urgency (2)				

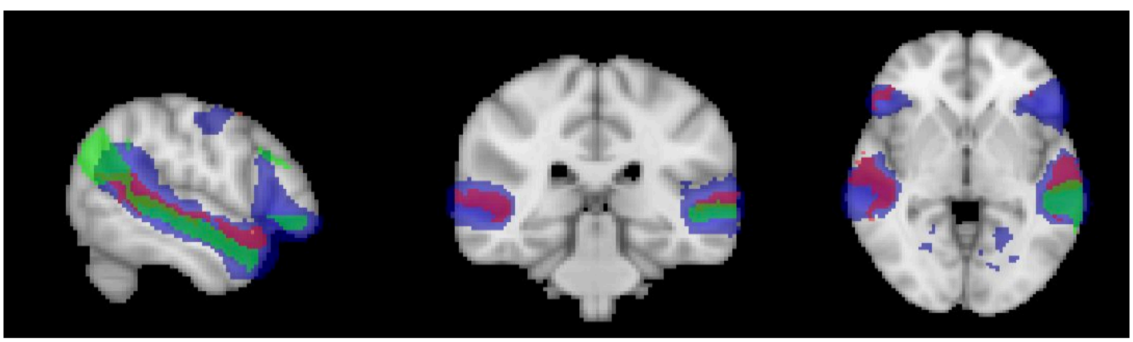
* indicates the measure used as a general index of disinhibited externalizing.

Lastly, it is important to mention that Study 2 was conducted using data collected during the MSIT task. I hypothesized that functional connectivity metrics computed from task data (from a task that may help elicit behavior relevant to the traits of interest) would show similar associations as during rest. However, results were not similar across Studies 1 and 2 (although given other differences, we cannot conclude this was specifically due to the distinction between task and rest data). As seen in Table 4.1, GPN coherence was associated with externalizing measures during task-based functional scans while CEN coherence was associated with externalizing measures during resting-state functional scans. This warrants more research in the future.

A DN subsystem appears to be related to Conscientiousness. Previous research on the neural correlates of Conscientiousness has found that a component in the default network is associated with Conscientiousness (Rueter et al., 2018). In this previous work, coherence in a component comprising the superior temporal gyrus and the temporal parietal junction was negatively associated with Conscientiousness (partial r = -.17, p = .017). While this finding did not hold after accounting for multiple comparisons, it is worth mentioning because both of the current studies found associations between DN networks and the Conscientiousness–disinhibited externalizing spectrum.

In both Study 1 and Study 2, components resembling part of the dorsal medial subsystem of the DN were both associated with Conscientiousness. The component in Study 1 included portions of the GPN (dlPFC), while Study 2's DN component appeared to exclusively reflect the DN. See Figure 4.1 below for a visualization of the overlap between Study 1 and Study 2 components.

Figure 4.1. DN components from Study 1 and Study 2.



Note. Blue components reflect the dorsal medial prefrontal cortex subsystem from Study 2. Green components reflect the right lateralized dorsal medial prefrontal cortex subsystem from Study 1. Red components reflects the temporal DN network from Yeo et al. (2011) 17-parcellation.

In Study 1, coherence in the DN component comprising the right lateralized precuneus and the posterior cingulate cortex (in green above) was positively association with Conscientiousness (partial $r = .07$, $p = .029$). This effect remained significant when controlling for the other Big Five traits. In Study 2, connectivity in a similar component was negatively associated with Conscientiousness (partial $r = -.26$, $p = .012$). This is puzzling because these ICNs appear to be reflecting the same network (albeit one is bilateral) yet they are showing opposite relations with Conscientiousness. This subnetwork has been shown to be activated when individuals make self-referential decisions about their present situation or mental states. Thus, it's function and relation to personality may change dramatically depending on the task that was completed in the scanner. In Study 1, individuals underwent a resting state fMRI scan while in Study 2, individuals were completing an inhibition task. It is possible that during rest, connectivity in this subsystem is more likely associated with Conscientiousness while during task the DN is less active. More research on the specific subsystems of the DN may help elucidate the relation between the DN and the Conscientiousness-disinhibited externalizing spectrum. Note, however, that this result could also simply be a result of type I error, with one or both of the detected associations being due merely to sampling variability.

Future directions. While there is relatively little fMRI research incorporating both Conscientiousness and disinhibited externalizing spectrum into a single study, there are many researchers who have used functional connectivity research to gain insights into neural networks associated with behavioral outcomes associated with ADHD and substance use. In the future, it would be beneficial to conduct a study with rigorous measures of personality in addition to collecting enough neural data (increasing both participants and length of scans) from both resting state fMRI and task-based fMRI scans. Large scale, publicly available datasets are useful but sometimes less than ideal given suboptimal measures. Smaller scale, local studies lack funding to scan a large number of participants for longer than 15 minutes across multiple tasks. Thus, these two types of studies are in conflict when it comes to reliability. When methods differ, reliability and replicability are reduced. When future large-scale studies are being conducted, it would be worthwhile to ensure that the best measures are included in the study to ensure the ability to replicate previous results. It would also be worthwhile to conduct a larger study on how neural networks and functional connectivity within neural networks change depending on the task that is completed in the scanner.

Understanding the neural correlates of the Conscientiousness-disinhibited externalizing spectrum is useful when attempting to understand why some individuals are able to accomplish their goals while others fall prey to impulsivity. This spectrum influences behaviors that affect everyone. Many life goals rely on acting in Conscientious ways while reducing disinhibited behavior. Some examples include being able to save money to buy a house, studying with ample time to do well on exams, and successfully applying for jobs. In the current self-help climate that emphasizes the many ways to better oneself, having high levels of Conscientiousness is coveted while impulsively spending one’s savings, cramming for exams, and putting off stable careers is detrimental. When we are better able to understand where these impulses, goal attainment, and self-control stem from, we will be better equipped to be successful in our lives through the development of interventions. The brain (including its patterns of functional connectivity) is malleable (Vaidya & Gordon, 2013), and it is entirely possible that people can improve their levels of Conscientiousness, increase their goal attainment, and start living a life they are satisfied with in the process.

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Appendices

Appendix 1. The UPPS Impulsivity Scales (Whiteside et al., 2005).

Below are a number of statements that describe ways in which people act and think. For each statement, please indicate how much you agree or disagree with the statement. If you **Agree Strongly** circle **1**, if you **Agree Somewhat** circle **2**, if you **Disagree somewhat** circle **3**, and if you **Disagree Strongly** circle **4**. Be sure to indicate your agreement or disagreement for every statement below. Also, there are a few more questions on the next page.

1. I have a reserved and cautious attitude toward life.
2. I have trouble controlling my impulses.
3. I generally seek new and exciting experiences and sensations.
4. I generally like to see things through to the end.
5. My thinking is usually careful and purposeful.
6. I have trouble resisting my cravings (for food, cigarettes, etc.).
7. I'll try anything once.
8. I tend to give up easily.
9. I am not one of those people who blurt out things without thinking.
10. I often get involved in things I later wish I could get out of.
11. I like sports and games in which you have to choose your next move very quickly.
12. Unfinished tasks really bother me.
13. I like to stop and think things over before I do them.
14. When I feel bad, I will often do things I later regret in order to make myself feel better now.
15. I would enjoy water skiing.
16. Once I get going on something I hate to stop.
17. I don't like to start a project until I know exactly how to proceed.
18. Sometimes when I feel bad, I can’t seem to stop what I am doing even though it is making me feel worse.
19. I quite enjoy taking risks.
20. I concentrate easily.
21. I would enjoy parachute jumping.
22. I finish what I start.
23. I tend to value and follow a rational, "sensible" approach to things.
24. When I am upset I often act without thinking.
25. I welcome new and exciting experiences and sensations, even if they are a little frightening and unconventional.
26. I am able to pace myself so as to get things done on time.
27. I usually make up my mind through careful reasoning.
28. When I feel rejected, I will often say things that I later regret.
29. I would like to learn to fly an airplane.
30. I am a person who always gets the job done.
31. I am a cautious person.

32. It is hard for me to resist acting on my feelings.
33. I sometimes like doing things that are a bit frightening.
34. I almost always finish projects that I start.
35. Before I get into a new situation I like to find out what to expect from it.
36. I often make matters worse because I act without thinking when I am upset.
37. I would enjoy the sensation of skiing very fast down a high mountain slope.
38. Sometimes there are so many little things to be done that I just ignore them all.
39. I usually think carefully before doing anything.
40. Before making up my mind, I consider all the advantages and disadvantages.
41. In the heat of an argument, I will often say things that I later regret.
42. I would like to go scuba diving.
43. I always keep my feelings under control.
44. I would enjoy fast driving.
45. Sometimes I do impulsive things that I later regret.

Scoring Instructions

This version of the UPPS Impulsive Behavior scale uses a 1 (agree strongly) to 4 (disagree strongly) response format. Because the items from different scales run in different directions, it is important to make sure that the correct items are reverse-scored. I prefer to make it so that all of the scales run in the direction that higher scores indicate more impulsive behavior. Therefore, I am including the scoring key for (lack of) Premeditation, Urgency, Sensation Seeking, and (lack of) Perseverance. For each scale, I prefer to calculate the mean of the available items; this puts them on the same scale. I usually require that a participant have at least 70% of the items before calculating a score for them.

(lack of) Premeditation (no items are reversed)

items 1, 5, 9, 13, 17, 23, 27, 31, 35, 39, 40.

Urgency (all items except 1 are reversed)

items 2 (R), 6 (R), 10 (R), 14 (R), 18 (R), 24 (R), 28 (R), 32 (R), 36 (R), 41 (R), 43, 45 (R)

Sensation Seeking (all items are reversed)

items 3 (R), 7 (R), 11 (R), 15 (R), 19 (R), 21 (R), 25 (R), 29 (R), 33 (R), 37 (R), 42 (R), 44 (R)

(lack of) Perseverance (two items are reversed)

items 4, 8 (R), 12, 16, 20, 22, 26, 30, 34, 38 (R)

(R) indicates the item needs to be reverse scored such 1=4, 2=3, 3=2, and 4=1

Appendix 2. DSM-IV ADHD Symptoms Scale.

Ratings before age 7: 0 = never, 1 = sometimes, 2 = often
Ratings current: 0 = never, 1 = sometimes, 2 = often

1. Fail to give close attention to details, or make careless mistakes.
2. Have difficulty sustaining attention in tasks or work activities.
3. Do not seem to listen when spoken to directly.
4. Do not follow through on instructions and fail to finish work.
5. Have difficulty organizing tasks and activities.
6. Avoid, dislike, or am reluctant to engage in tasks that require sustained mental effort.
7. Lose things necessary for tasks or activities.
8. Easily distracted.
9. Forgetful in daily activities.
10. Fidget with hands or feet or squirm in seat.
11. Leave seat frequently, difficulty remaining seated.
12. Subjective feeling of restlessness (as a child very active).
13. Difficulty engaging in leisure activity quietly.
14. Feel “driven by a motor,” always “on the go.”
15. Talk excessively.
16. Blurt out answers before questions are completed.
17. Difficulty waiting turn.
18. Interrupt or intrude on others.